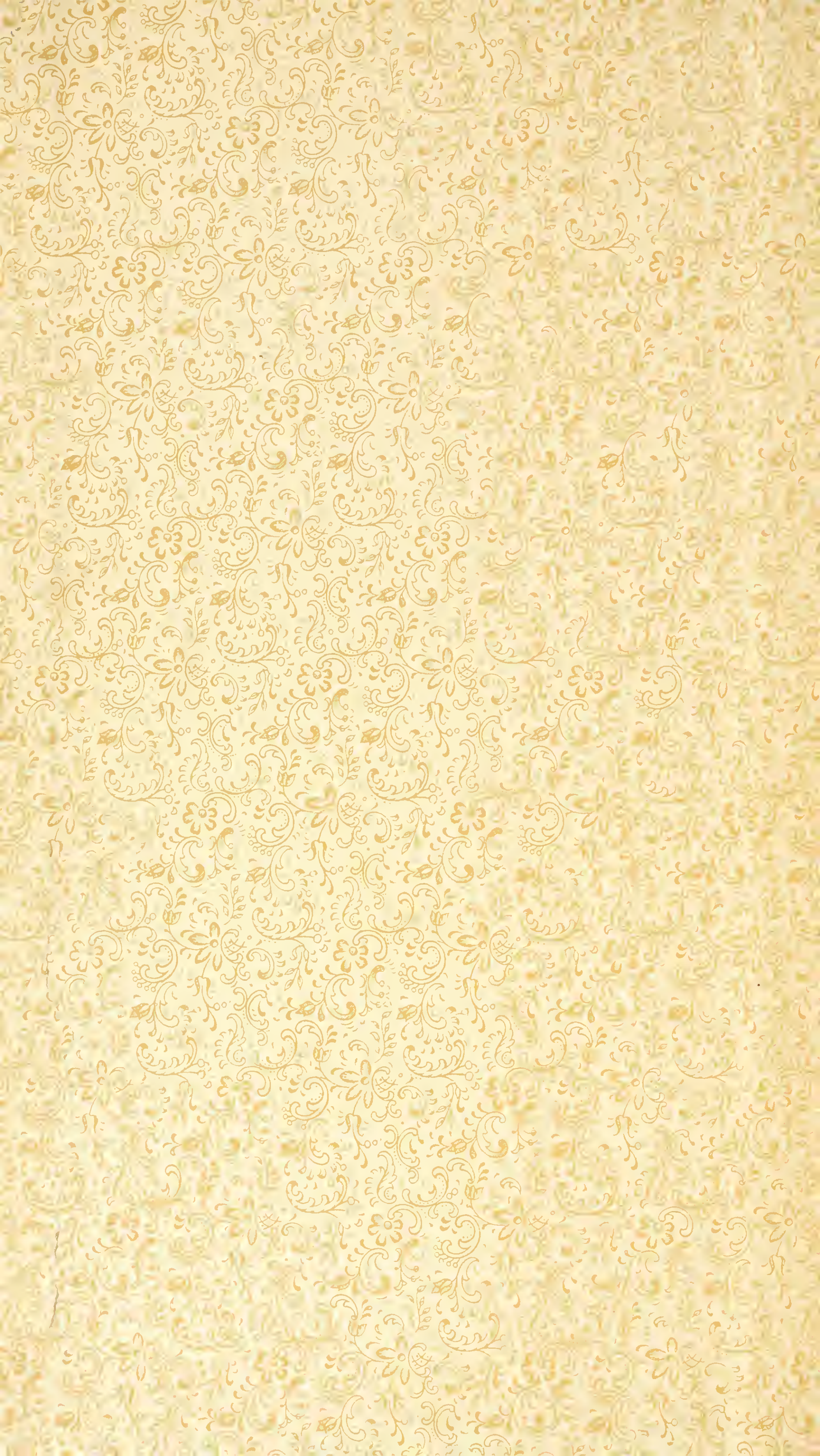

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In the references the letter [B] after the title signifies that the original memoir contains a good bibliography of the subject dealt with.

REVIEWS

DISEASES OF THE BLOOD

The blood in health and various morbid conditions. As the result of 95 examinations of the blood in children, Lesné and Langle came to the following conclusions: (1) the curve of digestive leucocytosis in children is subject to great variations, and it is very difficult to lay down a law applicable to all cases; (2) the ingestion of peptone has an inhibitory action on leucopenia, probably by modifying the colloid state of the blood; (3) excess of sugar in the milk has a similar effect, and acts by stimulating the hepatic functions; (4) digestive leucocytosis differs in the breast-fed and in the bottle-fed baby, the homogeneous albumin of the mother's milk being better tolerated than the heterogeneous albumin of cow's milk; (5) in under-nourished children leucopenia is constant even after ingestion of very small quantities of milk. It is also found in infective purpura and malignant diphtheria, and is constantly present in the serum disease.

Dorlencourt, Banu, and Paychère, state that in the normal infant more or less considerable changes invariably occur in the leucocyte count in the hours following a feed. In typical cases the most frequent succession of events is as follows: (1) sudden, pronounced, and transient leucopenia; (2) increase in number of leucocytes of slight intensity and short duration; (3) diminution in their number of slight intensity and longer duration; (4) sudden well-marked transitory hyperleucocytosis (true digestive leucocytosis; (5) return to the normal condition. Digestive leucopenia in the infant appears to be a normal phenomenon, whereas in the adult it is a pathological condition, according to Widal's researches. The test of digestive haemoclasia is therefore of no value in the infant.

Mauriac and Cabouat state that variations in the normal leucocyte count are due to numerous causes, such as the erect or recumbent position, examination of blood from the finger or the ear, a state of fasting or digestion, apnoea or amplitude of the respiratory movements, each of these factors being sufficient to change the blood formula. During their army service the writers made repeated examinations of their own leucocytes from 8 am. to 8 pm., as many as 23 examinations being made on the same subject in the course of the day. They were leading a quiet life at the time and taking the ordinary diet of an officers' mess. Their results were as follows: (1) In the normal individual the number of leucocytes varies from one moment to another. (2) The variations are least marked on getting up in the morning and are most pronounced from 3 pm. to 9 pm., during which time the total number of leucocytes may range from 12,300 to 6,500 in the course of half an hour. The widely different estimates of digestive leucocytosis are thus explained, for according to the hour, or rather the moment, at which the blood is taken there may be a leucopenia or a leucocytosis. The term 'digestive oscillations' is therefore preferable to that of 'digestive leucocytosis'. (3) The normal polymorphonuclear percentage showed great variations, ranging in one of the writers from 47 to 73 and in the other from 43 to 67. (4) The polymorphism, frequency, and suddenness of the changes in the leucocytes should make one very guarded as to their interpretation.

Hofferbert examined the blood of 30 men and 30 women, aged from 20 to 40, belonging to the medical and nursing staff of the Wiesbaden Municipal Hospital, and found an increase in the percentage of the lymphocytes at the expense of the polymorphonuclears. The lymphocyte count of 32·2 per cent. was not as high as that given by some recent writers, e.g. 36·6 or 40 per cent. (vide *Medical Science*, 1921, **5**, 3), but exceeded that given in ordinary text-books and works on haematology. Hofferbert also examined the blood of 30 patients, chiefly women, with a pronounced neurasthenic or hysterical condition, and found a lymphocytosis of 36·6 per cent. and an eosinophilia of 4·7 per cent.

Rodillon attacks the work of Pruche (vide *Medical Science*, 1920, **3**, 15), and in particular his statement that the sodium chloride content of the blood is a constant. Rodillon believes it to be eminently variable because: (1) this is proved by very numerous analyses by many different authors who are all agreed on this point; (2) this is in accordance with all that is known of the physiology and pathology of the kidneys; and (3) physiology and biology lead us to suppose that it could not be otherwise.

Ottenberg discusses the value of blood grouping in medico-legal cases. It is well known that all human beings belong to one of four blood groups characterized by their different combinations of two agglutinogens which we can call A and B. Thus we have Group I with neither of them, Group II with A only, Group III with B only, and Group IV with both. The two specific agglutinabilities of red cells, which for convenience we speak of as if they were definite substances, 'agglutinogens', are in each case associated with equally specific agglutinins which are not usually present at birth but develop later. It is obvious that if a child is found to possess one or both of A and B, these must have been derived from one or other or both parents. If, for example, a child is found to possess B and the mother is A, while the alleged father is also pure A, it is apparent that the alleged parentage is not the actual one. On the other hand, if the mother possesses A and B but the father neither, the children may belong to any of the four groups, so that no conclusion as to parentage can be based on the blood group of the children if either of the parents possesses both A and B, or if each possesses one of them. Ottenberg recognizes the possible legal difficulties in the way of compelling persons to submit to blood examination, but considers that the blood grouping is of sufficient importance to justify a law enforcing such examinations in cases of disputed paternity, &c.

Buchanan takes serious exception to the following statement of Ottenberg: 'If the child's group is wrong for the two asserted parents, then one can say with absolute certainty that the child must have a parent other than one of those asserted.' Buchanan presents figures of various families showing the appearance in children of the third generation of a blood group which was apparent in a grandparent but latent in the parent. It would appear from these figures that no medico-legal significance of the sort suggested by Ottenberg can properly be attributed to blood groups.

Dyke, after describing his own technique for blood grouping, also refers to medico-legal applications and appears to support Ottenberg's view that certain properties of the blood (known as A and B in the literature) are dominants and cannot be absent from the children.

Bain, Edgecombe, Kidd, and Miller have investigated the effect on the blood-pressure and metabolism of certain electrical procedures in common use at spas, viz. the d'Arsonval high-frequency current, the diathermic current, and the Bergonié treatment. They conclude as follows: the results of the d'Arsonval current were a slight but definite reduction in systolic and diastolic pressures; a temporary trifling loss of haemoglobin; a more enduring fall of leucocytes; an increase in output of urea, followed by an increase in the output of total nitrogen. The diathermic current may be said to cause a slight fall in systolic blood-pressure, an increase in leucocytes, and an increase in urea and ammonia nitrogen. The effects of the Bergonié treatment were as follows: the current without heat causes a slight rise in haemoglobin value; when heat is added a marked fall takes place (about 5 per cent.). The current alone causes a considerable rise of blood-pressure, which is converted into a fall when heat is added. There is a distinct effect in the direction of increasing metabolic changes. These findings are all deduced from experiments on the same three healthy persons, aged 64, 49, and 35 respectively.

Mottram has studied the blood changes as an index of the effects of exposure to radium, and concludes: (1) that a single blood examination may give a warning of danger if the count be near the lower limit for normals; (2) a considerable fall with a sustained low level indicates that insufficient protection is being given; (3) if several workers in the same department present low counts the indication is similar; and (4) that in workers using soft rays special attention should be paid to the lymphocytes since these cells are more likely to be affected than the polymorphs.

Giraud and Parès call attention to certain observations which they have made on the influence of X-rays on the blood. Their interest appears to have been awakened by the peculiar reactions of a case of leukaemia of the ordinary myeloid type. This case has been followed for five years. When first under treatment, in December 1916, he had 176,000 white cells. By July 1917 he had only 11,500. Three months later he had 34,300, but his spleen was not palpable and his general condition excellent. Seen again in May 1920, he had an enormous spleen and the white cells numbered 125,000. Methodical X-ray treatment reduced the splenomegaly very considerably, and the white cells fell to 35–40,000. The patient began again to lead an active life. Considerable pain over the spleen was also relieved by the X-rays. Up to this point the patient had always been easily tolerant of the treatment, but on his return to seek alleviation of a recrudescence of spleen pain it was found that his tolerance was failing. Each application was followed by transient but distressing symptoms, viz. nausea, malaise, respiratory embarrassment, vertigo, and vomiting. These lasted for some hours but never gave rise to any serious apprehensions. Similar crises have been described by German authors in both X-ray and radium therapy. The clinical features are accompanied by a sudden fall in the numbers of leucocytes, which rapidly fall to normal and a fall in blood-pressure. These are symptomatic of the 'haemoclasic crisis' of Widal and his school. There followed a more gradual fall in leucocytes, such as is expected in this disease and is presumably due to leucocytolysis. Giraud and Parès see in this case an example of auto-sensitization to the products of the X-ray lysis of blood-forming tissues and suggest the usual course of a minimal desensitization dose of rays in those who develop this sensitization.

Minot and Smith have considered the blood changes in tetrachlorethane workers from the point of view of early diagnosis. They consider a progressive increase of large mononuclear cells, often reaching 40 per cent., the most important sign. If these are much broken and degenerate the poisoning is likely to be more severe. Since such changes can be detected before the onset of clinical signs, they afford a means of putting employers and employees on their guard before permanent harm is done. But not every one who shows such changes will necessarily progress to the later stages of poisoning.

Nicloux reports a case of carbon monoxide poisoning in which complete recovery ensued within a few hours, although the proportion of carbon monoxide haemoglobin had presumably reached from 60 to 70 per cent. When the patient was brought to hospital, after oxygen treatment with the pulmotor, the percentage was 41·3, and this treatment was maintained until recovery ensued. The first recovery of consciousness was followed, as is usual, by relapse, but on the following day the patient was normal and was discharged. Nicloux protests against the old theory that a red cell once combined with carbon monoxide was dead and useless and points out that the amount of this gas which is absorbed is strictly proportionate to the amount in the atmosphere and the amount of oxygen mixed with it. The case recorded is an eloquent witness to the truth of these views.

Daland concludes that lymphocytosis is an important sign of peri-apical dental infection. He bases this view on the fact that in 100 cases of such infection the lymphocytes exceeded 38 per cent. in 54, whereas in 100 cases free from any focal infection, but suffering from chronic disease, only two showed lymphocytosis.

Blatteis contributes the following very short account of a remarkable case. A man, aged 45, gave a history of having just passed through an attack of influenza, and possibly of endemic typhus. While under observation his leucocyte count reached 100,000, myelocytes 48 per cent., and eosinophils from 10 to 14 per cent. There was an enlarged liver and spleen and there were other findings suggestive of myelogenous leukaemia. The blood count returned to approximately normal, and the symptoms cleared up. Blatteis states that a study of this case leads to the conclusion that many so-called cases of leukaemia are, after all, only cases of infection presenting an unusual leucocytosis.

Gänsslen examined the blood of 42 cases of migraine, and found that 31 showed an eosinophilia ranging from 5 to 16 per cent. In 11 cases the percentage was about normal, but several of these patients were suffering from another disease as well.

Anaemias of childhood. Thursfield classifies the anaemias of childhood into three main groups, as (1) congenital, (2) secondary, that is, those in which a removable cause is operating to produce the anaemia, and (3) primary, those in which an unknown, and at present usually unascertainable, cause is operating. In the first group only congenital acholuric jaundice is given a definite place. Von Jaksch's disease is considered a secondary anaemia, as well as all those due to sepsis, &c. In the third group Thursfield places, in order to invite discussion, only three diseases, namely, leukaemia, purpura, and 'anaemia gravis', by which term he prefers to denominate what is commonly called aplastic anaemia. It is obvious that certain well-known diseases of childhood do not receive a definite place in this scheme. Of these Thursfield remarks that haemophilia and haemophilia neonatorum seem to him to be examples of tissue diseases in which the haemopoietic function is secondarily disturbed.

Halbertsma, of Leyden, reports a case of anaemia pseudo-leukaemica infantum in female twins aged eight months, the principal facts in their history being premature birth, mother's anaemia, double otorrhoea, and rickets. Their blood picture showed nucleated red cells and myelocytes with an increased number of leucocytes. The child most severely affected was transfused with his father's blood, and the other child was treated with arsenic and iron, the diet being the same in both cases. At the end of four months the child treated by transfusion showed a much better general condition and an improvement in her rickets, whereas, in the other child the rickets was aggravated. The former child also showed a much better condition of the blood, not only as regards the haemoglobin content and the number of the red cells, but also as regards the occurrence of myelocytes and nucleated red cells, and also a diminution in the size of the spleen, whereas in the other child the blood condition had become worse and the spleen had increased in size.

According to Stoeltzner, director of the children's clinic in Halle, feeding with goats' milk is frequently followed by severe haemolytic anaemia in infants. The cause of this anaemia, according to Stoeltzner, is to be found in the soluble fatty acids of goats' milk. Discontinuance of goats' milk and the substitution of a mixed diet produce a cure of the anaemia provided that severe complications have not arisen. Goats' milk anaemia occurred in rickety children in the form of anaemia pseudo-leukaemica and in non-rickety subjects as simple anaemia.

Encouraged by the favourable results obtained by Czerny and Eliasberg in tuberculous cachexia by protein therapy (vide *Medical Science*, 1921, **3**, 502), Behrendt, of Dortmund, treated 7 cases of severe anaemia in children aged from five months to three years by intramuscular injections of serum (ordinary horse serum or a specific serum such as antimeningococcic, or antitetanic serum) in daily doses of 1 c.cm. The smallest number of doses given was 11, and the largest 45. In five cases a more or less considerable rise in the haemoglobin value and number of red cells took place, as well as an improvement in the general condition. In the remaining two no change in the blood picture ensued, although the general condition showed considerable improvement.

Chlorosis. Schauman publishes five charts showing how greatly the frequency of chlorosis varies from time to time. The first chart deals with the number of cases treated at the Sabbatsberg Hospital in Stockholm in the period 1879–1903. In 1882 these cases numbered 5, and in 1892 they numbered 68. Between these extremes there were figures showing that, apart from slight annual fluctuations, there was a steady rise from 1882 to 1892, and a steady fall from 1892 to 1903. The second chart deals with the same hospital and covers the period 1904–19. From 1904–13 there was not a single case, and the rise, which culminated in 1916 with the small total of 6 cases, subsided in a couple of years to an average of 1 case a year. The remaining three charts, which deal respectively with the Sahlgrenska

Hospital in Gothenburg (1891–1919), the Massachusetts General Hospital (1898–1906), and Schauman's hospital in Helsingfors (1897–1920) show the same remarkable fluctuations. It is probable that they do not depend on the caprices of hospital physicians, whose inclination to give chlorosis hospital treatment may vary considerably from time to time, for many general practitioners have observed great dwindling in the frequency of chlorosis during the last few years. Schauman finds it difficult to provide an adequate explanation for the periodicity of this disease, but he is inclined to suspect that an interplay of heredity and alcoholism with disturbances of the internal secretions may determine the outbreak of chlorosis. He refers to a work by Magnus Huss in 1852, on the endemic diseases of Sweden, in which the author correlated the excessive consumption of alcohol in 1830 with the remarkable frequency of chlorosis in 1850. Schauman points out that it is difficult to verify a theory connecting injury by alcohol to the germ cells of the parent with an outbreak of chlorosis in the offspring a score of years later, for many of the available statistics bearing on this point deal with a period when the diagnosis of chlorosis was on a less sure footing than it is at present. But he thinks the explanation he has suggested is sufficiently plausible to warrant further investigation.

According to Salzman, of Toledo, Ohio, chlorosis is not a primary anaemia, but is due to a non-specific toxaemia which is the result of a focus of infection in the tonsils. He attributes the beneficial action of iron to its ability to combine with the toxin, producing a harmless organic compound, whereby the anaemia is prevented and the general condition improved, though a permanent cure can be effected only by removal of tonsils and elimination of the focus of infection.

Aplastic anaemia. Benoit, of Montreal, records a case of aplastic anaemia in a man aged 44, which presented the following features of interest: (1) The autopsy showed merely an excessive anaemia without any obvious lesion to account for it. (2) Examination of the blood showed an intense anaemia (haemoglobin 30 per cent., red cells 1,325,000) and a complete absence of a defensive reaction. (3) Intense haematuria without any renal lesion. (4) Absolute failure of treatment. Benoit suggests that the development of this rare form of disease was favoured by a constitutional predisposition, viz. familial tuberculosis.

Moore and Keidel, of the Johns Hopkins Hospital, report a fatal case of stomatitis and aplastic anaemia due to neo-arsphenamine in a woman aged 50, and have found only three similar cases on record, described by Labbé and Langlois, Esbach, and Görke respectively. The writers maintain that reactions of this type are by no means so rare as the few reports in literature would indicate, as they have found that damage to the bone-marrow, as shown by changes in the blood picture, is present in the majority of patients reacting to arsenical drugs with a rash of the dermatitis exfoliativa group, and that these blood changes differ only in degree from the severest reaction which was exemplified in their case.

Williams reports two cases of aplastic anaemia for comparison with those cases which have been noted in radiologists. The first case was that of a man, aged 45, who had worked in trinitrotoluol manufacture. He died between three and four months after ceasing to be exposed. The bone-marrow was yellow and consisted of fat and lymphoid foci. The liver was much scarred and the spleen was normal. The second case was that of a married woman, aged 41, who had worked in T.N.T sheds for twelve weeks. The post-mortem findings were similar to those of the first case. Comparison with the results of X-rays shows a very close parallel in symptoms and in the blood and marrow changes.

Pernicious anaemia. Levine and Ladd studied 150 consecutive cases of pernicious anaemia at the Peter Bent Brigham Hospital, Boston, U.S.A., with the following results: (1) Persistent absence of free hydrochloric acid was practically constant, being noted in 99 per cent. of the cases. This was often present years before the blood showed any typical changes and possibly always antedated them. It was therefore of considerable importance in diagnosis. (2) There seemed to be a distinct familial factor in pernicious anaemia. In nine patients there was a definite family history of the disease in some other member of the family, and in two others there was a history of death from an unknown type of anaemia. (3) The incidence of the disease was greater in English-speaking people and Scandinavians than in immigrants from Russia, Italy, and Eastern Europe. (4) Syphilis played no significant rôle in the series. Of 143 patients only 6, or 4·3 per cent., gave a positive Wassermann reaction, which was about one-third the percentage of positive Wassermann reactions in all medical patients admitted to the hospital. When the Wassermann reaction was positive, antisyphilitic treatment did not alter the course of the anaemia. (5) Eosinophilia was frequent. Of 143 patients 54 showed 5 per cent. or more at one time or another. Even a very high eosinophilia—25 per cent. or more—was not incompatible with the disease. (6) The proportion of males to females was 2 to 3. The average age of both sexes was about 51 years.

Owing to the rarity of pernicious anaemia in childhood (vide *Medical Science*, 1921, **3**, 394–5), mention should be made of Condat's case, which occurred in a girl aged 14. The onset took place a few months after the establishment of menstruation, and death ensued after barely two months' illness.

Of 30 cases of pernicious anaemia examined by Biffis in Ceconi's clinic at Turin, 7 were in women, in 5 of whom the condition could be attributed to pregnancy and the puerperium, and 23 were in men, among whom the only possible causes were *Bothriocephalus* in two, malaria in two, and syphilis in one. Biffis's conclusions are as follows: (1) Changes in the mouth in pernicious anaemia such as stomatitis and glossitis are rare in Italy and should be regarded as a consequence and not the cause of the disease. (2) Achylia gastrica may be absent in very rare cases. It occurs later than the changes in the blood and may be regarded as the result of congenital or acquired weakness of the stomach, or of its secretory or nervous apparatus. In any case it is not the cause of the anaemia. (3) Rapid emptying of the stomach, which is very frequent in pernicious anaemia, is due not to gastric hypermotility but to pyloric insufficiency, while the very rare phenomenon of pyloric spasm should be regarded as vagotonic. (4) The occurrence of diarrhoea in pernicious anaemia is difficult to explain, but it may possibly be due to absence of hydrochloric acid in the gastric juice.

Sakheim reports a case of pernicious anaemia in a woman aged 51, in whom during life and at the autopsy *Ascaris lumbricoides* was found in such large numbers that the possibility of their being the cause of the condition seemed probable. He refers to three similar cases reported by Gomess in 1907.

Maynard and Sturton record two cases of pernicious anaemia with infective foci in the alimentary tract. In the first patient, a woman aged

38, there was a history of colitis and the autopsy showed a definite ring o ulcers in the ileum. In the second patient, a man aged 58, there was an infective focus in the teeth. Recovery followed extraction of the teeth and treatment by novarsenobillon and an autogenous vaccine.

According to Zadek, of the Neukölln Municipal Hospital, the clinical and haematological signs of pernicious anaemia, though attenuated, are usually quite distinct during a remission. On the other hand, cases may occur with well-marked periods of remission, of which Zadek records four examples, in which the only characteristic clinical symptoms which persist are those due to irreparable organic changes, such as cardiac degeneration with oedema, achylia gastrica, necrosis of the tongue, spinal cord lesions, &c. The characteristic changes in the blood are absent during this period, and the bone-marrow is yellow and free from erythroblasts. The remissions are therefore not produced by megaloblastic regeneration which is completely absent in the bone-marrow and the blood, but are caused by a cessation in the production of toxins.

Menninger reports a case in a man aged 62, in whom, as in Curschmann's patient (vide *Medical Science*, 1921, **3**, 395), the symptoms of spinal cord disease antedated those of pernicious anaemia. The nervous condition, which was mistaken for tabes, was really ataxic paraplegia. A relatively favourable prognosis as to life was given, as the progress of the anaemia, as well as the spinal cord changes, was very slow.

Kretschmer, of Chicago, who records four personal cases, draws attention to the occurrence of bladder and urinary changes in pernicious anaemia which are apparently due to lesions in the spinal cord and a superadded infection. Their degree depends upon whether the patient is seen early or late in the course of the disease. At an early stage difficult urination suggests obstructive lesions at the neck of the bladder. As the disease progresses, bladder weakness develops, and later incontinence, with complete bladder paralysis in the terminal stages. In some cases there is incontinence of faeces as well as urine.

Peters and Rubnitz, of Omaha, examined blood from three series of persons for its concentration in (*a*) total solids, (*b*) total nitrogen in whole blood, (*c*) total nitrogen in plasma. The first series comprised physiologically normal persons ; the second, cases of pernicious anaemia and severe secondary anaemia ; and the third, cases of various pathological conditions other than severe anaemia. They found that the total solids of pernicious anaemia and also of severe secondary anaemia showed a great decrease from normal values, and even from that of other chronic hospital cases. The increase was due primarily to the large diminution in number of the red corpuscles and only in minor degree to decrease in plasma solids. The total nitrogen in whole blood in pernicious anaemia and also in severe secondary anaemias showed, like the total solids, a great decrease from the normal values, the principal causes being there also a diminution in number of the red corpuscles. The total plasma nitrogen in contradistinction to the total blood nitrogen either maintained its normal limits of constancy or tended to increase in percentage above that of most normal bloods, but in any case it had no tendency to decrease its nitrogen value. The writers conclude that since in all anaemic conditions the whole-blood nitrogen decreases while the plasma nitrogen tends to increase, the resultant ratio of the first to the second, which constitutes a nitrogen index, shows from the direction of variation in both factors a natural tendency to diminish in proportion to the severity of the anaemia. This index may be used as an indicator of the state and progress of the anaemia.

Denny, of Boston, U.S.A., determined the total blood-volume of ten patients who were transfused for pernicious anaemia, and found that it was reduced in all but two cases. The plasma volume remained essentially normal, the decrease in total volume being due to loss of cell-mass. There was no noticeable relation between the severity of the disease and the decrease in total volume.

Flater, of Stettin, remarks that though the value of the blood picture is incontestable in the diagnosis of pernicious anaemia, it is not always justifiable to draw conclusions therefrom as to the course of the disease. Although as a rule the blood picture corresponds to the clinical course, cases may be found in which this parallelism does not occur. Flater reports an example in a man, aged 63, in whom, as the result of arsenical treatment, the haemoglobin rose to 81 per cent., although the presence of oedema, pleural effusion, and haemorrhages showed the hopelessness of the condition. Even at the time of death the haemoglobin was still 58 per cent., and the red corpuscles numbered over 2½ millions, whereas death in pernicious anaemia is usually accompanied by an extreme degree of anaemia.

Böttner and Werner, of the Königsburg Medical Clinic, obtained good results in six cases of pernicious anaemia by duodenal lavage, which they regard as the best method of removing toxic products from the intestine. The fluid used consisted of sodium chloride 9·0 gm., sodium sulphate 9·0 gm., and water 750–1,000 c.cm.

Hunter further elaborates his views on the severest anaemias and makes an eloquent plea for the abandonment of the misleading title 'pernicious' in connexion with one of them. In his experience glossitic lesions are so frequent, so early, and so important from a diagnostic point of view that the term 'glossitic' should replace 'Addisonian' or 'pernicious' in the nomenclature of the disease. Hunter now proposes as the full name 'idiopathic glossitic anaemia'. From this disease he carefully differentiates septic anaemia, and points out the error of those who have credited him with the view that dental sepsis can cause the glossitic type. The fact is that the two sometimes co-exist, and in such cases the eradication of the septic element gives the body defences a greater chance of dealing with the idiopathic glossitic anaemia.

Hunter emphasizes the fact that when septic factors are removed the recovery from glossitic anaemia is extraordinarily hastened. His large experience seems to leave no doubt of this.

Leukaemia. Sabrazès (1) states that contrary to the view held by A. Fraenkel in 1895 there are different types of acute leukaemia, and it is erroneous to suppose that there is only one form of acute leukaemia with so-called undifferentiated cells. The forms in which megaloblasts predominate are the most malignant and prove fatal in a few days. The lymphoplastic forms are fatal in a few weeks, and the myelocytic or lymphocytic types, in which the cells are nearer maturity, in two or three months. In acute myeloid leukaemia the disease may last a year. In every case there is anaemia, which is often severe, and, in the exceptional instances of the pernicious type, frequently accompanied by a haemorrhagic syndrome. In some cases the disease resembles ordinary acute leukaemia owing to enlargement of the spleen and lymph glands and the pain on pressure on the sternum, but the course is more rapid, the tendency to haemorrhages more pronounced, and the asthenia profound. Acute leukaemia may be mistaken for septicaemia, typhoid fever, dysentery, acute or subacute pulmonary tuberculosis, purpura haemorrhagica, scurvy, acute rheumatism, or acute nephritis. Sometimes the disease is complicated from the first by haemorrhagic and gangrenous processes in the pharynx, buccal mucosa, and gums, and may simulate toxic diphtheria. Various pathological conditions figure in the history, such as rickets, chronic enteritis, septicaemia, puerperal infection, typhoid fever, scarlatina, tuberculosis, malaria, syphilis, and influenza, but usually they should be regarded as antecedents rather than causes. On the other hand, traumatism has more aetiological importance and deserves more attention from the clinical and medico-legal standpoint. Treatment has hitherto proved unavailing. The measures employed in chronic leukaemia, such as radium, X-rays, benzol, &c., are inoperative or contra-indicated in chronic leukaemia.

Kaltenbach reports very fully a case of acute leukaemia in a man of 30. The type of cell showed that the disease was of the myeloid group, but a majority of the cells were less developed even than myelocytes. At autopsy there were found ulceration of the larynx and of the small intestine as well as the more usual findings. The intestinal ulceration affected the free edges of the valvulae conniventes, and the long axis of the patches of ulceration was parallel to these valves. Three guinea-pigs were injected with material obtained at autopsy, but no result on their health was observable.

Reh reports a case in a boy aged 9, which he asserts to be an example of lymphatic leukaemia originating solely in the bone-marrow. Clinically, there were the usual features of an acute leukaemia, except that no enlargement of glands or spleen could be detected. The leucocytes were but little increased in numbers, and the case was at first supposed to be one of aplastic anaemia, as happened in the case of Gunewardene (vide *Medical Science*, 1920, **3**, 20). Subsequent developments did but little to make the nature of the case more evident, and it was not until autopsy that a satisfactory diagnosis was arrived at. The spleen was found slightly enlarged, but no account of its microscopical appearance is given. The glands were not affected with leukaemic changes. There were small leukaemic foci in the bladder and on the dura mater, and the kidneys showed the usual infiltration. If the cells described as lymphocytes in this communication are indeed of this nature and not (as seems so much more likely) some ancestor of the myelocyte or common to both myeloid and lymphoid series, the contention of the author is almost established, and would be quite sound if the cause of the enlargement of the spleen was given. But no details are offered as to the appearance of the so-called lymphocytes, an omission fatal to general acceptance of the author's views.

Bonnamour and Chapuis report a fatal case of myeloid leukaemia and tuberculosis in a woman whose husband had died of meningitis. The autopsy showed an old tuberculous abscess in the liver and recent generalized miliary tuberculosis. They allude to a paper by Nanta in 1913, who recorded four cases of leukaemia with latent tuberculous lesions, in which acute tuberculosis subsequently developed.

Weil and Coste report a case of acute lymphatic leukaemia in a young man which tended to assume the chronic form. The total white cell count fell and the number of myeloblasts (although described as lymphatic on clinical grounds, this was an acute myeloid case) diminished. But the general condition of the patient did not improve and he died five months after the onset from generalized tuberculosis of the haemopoietic system. The presence of giant cells was not noted, but the tissues were full of bacilli morphologically and tinctorially identical with Koch's bacillus. Animal inoculation could not be done. It is noteworthy that Hirschfeld published a case with the same anomalies, and the authors write to suggest that more bacterial examination is needed in cases of leukaemia complicated by tuberculosis.

Lucas describes a special form of myeloid leukaemia which is characterized not only by enlargement of the spleen but also by enormous swelling of the lymph glands from the first, so that the condition clinically resembles lymphatic leukaemia. Although only a small number of cases have been published, Lucas thinks that many escape recognition or are regarded as lymphatic leukaemia owing to the clinical appearances. The disease usually runs a subacute course of eight to nine months. The diagnosis cannot be made clinically, but only by haematological examination. The treatment is the same as that of chronic myeloid leukaemia.

Gunderson, of the Harvard University Medical School, who studied the basal metabolism in nineteen cases of myelogenous leukaemia and its relation to the blood findings, found that the basal metabolism bore a relation particularly to the number of the immature white cells in the blood regardless of the total leucocytes. The highest values for the basal metabolism were usually found in cases with very high white counts and many myelocytes or in cases showing high percentages of myeloblasts. Gunderson considers that both these findings probably signify great activity of the leucopoietic tissue, and that the basal metabolism determinations should be considered as indices of this activity.

Sachs reports a fatal case of lymphatic leukaemia in a woman aged 65, who for two years before death had crops of a pemphigoid eruption on the face, trunk, and limbs, consisting of bullae filled with a clear or haemorrhagic fluid. The eruption was always preceded by intense hoarseness due to an enanthem in the larynx.

Bass has collected twenty-three cases of leukaemia in children from the records of the Mount Sinai Hospital, New York, of the past ten years. The cases showed that leukaemia in children is essentially an acute disease, as the longest duration of any of the cases was one year. All the cases which lasted more than a few months were of the myeloid type, chronic lymphatic leukaemia apparently not occurring in childhood. In six cases symptoms referable to the nervous system were prominent. Four of these gave the picture of cerebral haemorrhage, which was confirmed in one by autopsy and in two by lumbar puncture, one in which the clinical symptoms indicated leukaemic infiltration simulated cerebrospinal meningitis, and in one the terminal cerebral symptoms were found by autopsy to be due to leukaemic infiltration.

Other recent examples of leukaemia in children have been reported by Langsch (1) (myeloid leukaemia in children aged 9, 10, and 12 years), Salvetti (lymphatic leukaemia in a boy aged 3 years), Hess and Isaac (lymphatic leukaemia in a boy aged 3 years), and Langsch (2) (lymphatic leukaemia simulating mumps in an infant of 14 months). As the aetiology of leukaemia is still obscure, it is noteworthy that the disease developed after paratyphoid B infection in the case recorded by Hess and Isaac. One of Langsch's cases of myeloid leukaemia developed slight left facial paralysis and limitation of movement in the left hip probably due to leukaemic infiltration. In this connexion reference may be made to the cases recently reported by Aloi, Taddei, and Weber (1), of more or less massive haematomata on the trunk or limbs due to this cause.

Lindstroem has produced a leucotoxic serum by immunizing a sheep against rabbits' leucocytes. Intravenous injections of this serum produced in rabbits a fall in the total number of leucocytes and eventually death. In each case there was first a stimulation of leucocyte production. This was transient and occurred only with relatively small doses. These results were then applied to the treatment of the blood diseases in human beings. Two cases of pernicious anaemia were treated at the Sabbatsberg Hospital, Stockholm, with a serum leucotoxic and haemolytic for human blood. It was hoped that benefit might be obtained from the earlier stimulating effect. The results were negative. Four cases of myelaemia were then treated. In Case 1 treatment by X-rays had produced a remission, but this had not been lasting and the spleen had remained palpable. After the first injection of serum the patient had pain over the spleen and in the limbs. In the next fortnight the spleen enlarged further and the red cells fell. The next injection was followed by a serious advance of the disease, but very soon after the patient's condition improved so much that she expressed herself as being as well as she had ever been, and the white cells fell to normal numbers. Later still, there was a return of symptoms and the patient refused further serum injections. Case 2 was of a more acute type, but an injection of serum produced a speedy and remarkable remission. This lasted four months, when a relapse proved fatal in spite of a further injection of another serum. The two other cases suggest that the serum has an effect, but were not in any way conclusive. Lindstroem refrains from drawing any conclusions from so few cases.

Ruggeri reports at considerable length a case of leukaemia treated by injection of novarsenobenzol which gave rise on each injection to a haemoclasic crisis. The first part of his paper is devoted to a full statement of the clinical side of the case. Secondly, he details the blood examinations and the modifications brought about by each crisis. These were not very well marked, but were sufficiently typical to emphasize the nature of the clinical signs of crisis, cyanosis, sweating, increased pulse-rate, &c. The blood counts were anomalous in several respects, but, generally speaking, were of myeloid type. Ruggeri points out that the school of Widal have also described the haemoclasic crisis following non-protein injections, but it is possible that in this case the patient was sensitized to the products of his destroyed white cells as much as to the salvarsan. The case of Giraud and Parès should be read with this (*vide supra*, p. 5).

Schisler and Brown, of St. Louis, are of opinion that periodic treatment with combined benzol and X-rays can keep the leukaemic patient free from symptoms and definitely prolong life in the chronic form. They report a severe case of chronic myeloid leukaemia in a man aged 45, in whom combined benzol and X-ray treatment, constantly controlled by white cell and differential blood counts, gave a temporary and complete relief from symptoms and a satisfactory decrease in abnormal blood cells, the differential count approaching normal limits.

Hodgkin's disease. Lemon and Doyle, of the Mayo Foundation, record their observations on Hodgkin's disease in a paper based on the study of 26 cases. 17 were males and 9 females. Their ages ranged from 20 to

64. This is contrary to Reed's observation that children are most often attacked, and is probably due to the fact that relatively few children are admitted to the clinic. The writers do not believe that tuberculosis plays a part in the aetiology, and no other infectious disease was found that could be considered a cause. Enlarged glands were found in the cervical region in 100 per cent., in the supraclavicular region in 58 per cent., in the axillary region in 50 per cent., in the abdominal region in 19 per cent., and in the inguinal region in 42 per cent. Splenomegaly was discovered in 23 per cent., and involvement of the liver in 11 per cent. Blood counts were made in 23 cases, but no material changes from the normal were found. In addition to the ordinary measures, many patients were treated with radium, and the glands responded most satisfactorily. X-rays were used in a limited number of cases with good results, there being a replacement by connective tissue and a diminution in size of the glands.

Ribadeau-Dumas remarks that though comparatively few cases of Hodgkin's disease have been published in France the disease is not really uncommon, as he had himself found seven examples among 32 cases of enlarged glands of the neck examined by him at the Trousseau Hospital for Children in Paris, and since then had met with several other cases. The mediastinal form, of which he reports an example, may assume various appearances. There may be a number of symptoms of compression with little or no constitutional disturbance. Then at a later stage there develop enlargement of the supraclavicular glands, oedema, subcutaneous lymphomata, and pleurisy, indicating invasion of the pleura and lungs, and death takes places from cachexia. The course of the disease thus resembles that of a malignant tumour of the mediastinum. On the other hand, the onset may at first be that of an infective disease with fever, cutaneous eruptions, and glandular enlargement, signs of a mediastinal tumour not occurring till the last. Or again, the onset may at first be mistaken for that of an attack of pneumonia or acute pulmonary congestion. After a short stage of apparent improvement, symptoms of a severe infection develop, and the diagnosis of acute tuberculosis may be made. Ribadeau-Dumas insists on the diagnostic value of a biopsy, which, as in his own case, will reveal the true nature of the condition.

Langley reports a case of Hodgkin's disease in a man of 24. The earliest symptoms were enlargement of glands and appearance of many cutaneous nodules. Later, one of the latter broke down and ulcerated. Four months before death a mass appeared to grow from the second left chondrosternal junction and another from the lower cervical vertebrae behind. These were fixed and were probably periosteal growths, which are of very rare occurrence in this disease. No autopsy was permitted. It is noteworthy that X-ray treatment greatly diminished the size of the glands, but had no effect on the nodules in the skin.

Loygue describes at length a case of Hodgkin's disease combining some unusual, but by no means unexampled, clinical and pathological features. A soldier aged 20 was suddenly attacked with swelling of the glands in the right axilla and neck. There followed a long period of apparently typical Pel-Ebstein temperature, during which the glands varied in size. The spleen was found enlarged at the commencement of the disease and later the liver and the retroperitoneal glands were affected. The case is of interest in view of the theory that the primary involvement of cervical glands betokens a tonsillar portal of infection. In this case the spleen was already enlarged when the glandular condition appeared. *Post mortem* the spleen was of the 'hard-bake' variety and the glands were quite discrete. On one lung and one kidney were noted minute spots of a brownish colour. Both were found to be lymphoid foci not affected with any pathological lesion and perhaps in the nature of compensatory formations. Microscopy of the glands showed complete absence of eosinophils (which had also been absent from the blood during life) and here and there tubercular foci, but the general appearance was that of Hodgkin's disease. Loygue makes the suggestion that eosinophilia and cellular polymorphism are in reality less characteristic of Hodgkin's disease than the multinucleated cells and the general tendency of the tissues to sclerosis, and, he might have added, focal necrosis. He is evidently attracted by the suggestion that the commonly observed eosinophilia is rather a reaction to than a part of the disease process.

Fox reports a case which, he states, was clinically one of Hodgkin's disease, but which differed from the usual type in that the liver, spleen, and inguinal glands bore the brunt of the enlargements. The autopsy report suggests that the disease was primary in the spleen, or possibly in the abdominal glands. A further remarkable feature of the case was the presence of numbers of tubercle bacilli in the lesions which were otherwise typical of the Andrewes-Reed-Longcope type. In only two places was there any suggestion of tubercle giant cell systems, and both lacked the giant cell. In general, the bacilli were not the foci of any reaction. Fox does not draw any definite conclusions, but is evidently prepared to consider anew the relationships between Hodgkin's disease and tuberculosis.

Schiffner, of Vienna, reports a case of Hodgkin's disease in a woman aged 30, which had lasted eleven years with frequent relapses which always yielded promptly to X-ray treatment. He has been unable to find a record of any case of equal duration, though Mayer's case lasted seven years. Such cases always raise the question of the possibility of a permanent recovery, which all writers are agreed does not occur.

Samut, of Malta, records two cases of Hodgkin's disease successfully treated by colloidal manganese, three intragluteal injections being given weekly in each case.

Haemophilia. Rimbaud, of Montpellier, who remarks that meningeal haemorrhage is not a frequent cause of death in haemophilia, reports a case in a man aged 40, the subject of congenital haemophilia, who had presented several haemorrhagic manifestations in the course of his life, especially a relapsing haemarthrosis of the left knee followed by ankylosis. One night he was suddenly seized with a violent pain in the right fronto-parietal region and rapidly became comatose. There was no hemiplegia or localized paralysis, but only marked contracture of both upper limbs and a slow pulse (44). The diagnosis of meningeal haemorrhage was confirmed by lumbar puncture. No mention is made of an autopsy.

Sabrazès (2), of Bordeaux, records a case of haemophilia in an infant aged 18 months, who was still being breast-fed. There was no hereditary or familial history of haemophilia, and no other cause could be found except prolonged lactation to account for the condition.

Weil records the case of a bleeder whom he had treated for four years (1909–13) by injections of horse-serum every two months. During this period the patient was given fifteen injections, which caused a complete clinical cessation of all spontaneous or provoked haemorrhages. The patient belonged to a family in which the haemophilia had been known since the eighteenth century. He had first been given treatment at the age of 7, and for the last seven years had had none at all, so that his recovery might be regarded as permanent. Examination of the blood showed that both the qualities of the clot and the coagulation time were normal. Weil has treated seven other cases of familial haemophilia successfully by repeated doses of horse-serum (vide *Medical Science,* 1920, **2,** 149; 1921, **3,** 398).

Herzog, of Greifswald, who remarks that comparatively few cases of haemophilia treated by transfusion have been reported, records a case in a man aged 20 successfully treated by this method, the donor being the patient's sister.

Saint-Paul states that in cases of haemophilia, in which Nolf's method of subcutaneous injection of peptone is ineffective, X-ray treatment of the spleen should be tried. The whole spleen should be irradiated, and the maximum dose should not exceed one-third of the dose capable of irritating the skin. The irradiations soon cause a return of the normal coagulability of the blood and the haemorrhages cease. This result, however, is not permanent, and lasts only a few days. The patient therefore should be kept under observation and the irradiations repeated if necessary. Cases of severe haemorrhage with infection are refractory to this method. X-ray treatment should be accompanied by the ordinary measures for treating haemophilia.

Purpura. Rosenfeld, of Portland, U.S.A., describes two cases of idiopathic purpura, in brothers aged 11 and 15, presenting the following unusual features: (1) a familial tendency, (2) repeated joint haemorrhages in both cases, (3) association of joint haemorrhages with symptoms of Henoch's purpura, (4) spontaneous fracture of the olecranon in one case.

Thalimer reports the case of a boy aged 6 suffering from purpura. He was transfused from his father by the citrate method. Prior to the transfusion macroscopic and microscopic agglutination tests revealed absence of any incompatibility and of haemolysins. Somewhat over two weeks later symptoms returned and the boy was again transfused from his father, no blood tests being performed. When 150 c.cm. had entered the vein the boy became suddenly shocked, and his skin was peppered with bright red spots apparently from emboli composed of agglutinated 'foreign' red cells. Some hours later he had haemoglobinuria and the urine did not return to normal for three days. The lesson is plain that every possible test must be done every time or unfortunate results may follow blood transfusion.

Pittaluga describes four cases of purpura haemorrhagica, laying particular stress on the treatment adopted. He employed the following: (*a*) large doses of normal horse-serum by mouth and hypodermically; (*b*) the same with adrenalin; (*c*) Dufour's anaphylactic treatment; (*d*) intravenous human serum; (*e*) blood transfusion; (*f*) cholesterin and lecithin; (*g*) gelatin and serum with gelatin; (*h*) large hypodermic injections of isotonic glucose solution with tonics, cardiac stimulants, &c.; and (*i*) calcium chloride. He had negative results from Dufour's method, and found that intravenous injection of human serum was of little value owing to the difficulty of obtaining sufficient. He did not use peptone injections in this series having experienced untoward anaphylactic symptoms in previous cases. He admits their value in haemophilia, but considers that their efficacy depends on the integrity of the liver, a factor seldom to be depended on in such toxic cases as those of purpura haemorrhagica. He further considers that injections of camphor are made far too often as a matter of routine and without sufficient indication.

Dumas and Bernheim, of Lyons, record a case of purpura haemorrhagica in a woman aged 22, who had been subject to metrorrhagia—preceded by purpura every year since puberty, severe epistaxis taking the place of metrorrhagia before that date—since she was 3 years of age. With two exceptions, the haemorrhages always occurred in July and August. There was no case of haemophilia in the family, and the normal coagulation, ill-marked retraction of the clot, and absence of haematoblasts were characteristic of purpura and excluded the possibility of sporadic haemophilia. The patient also presented undoubted signs of tuberculous infection in the form of scars resulting from cold abscesses and multiple osteitis. The case was thus an example of chronic purpura of tuberculous nature which Bensaude and Rivet described in 1905.

Polycythaemia. From a careful study of the coagulability of the blood in five cases of erythraemia, Laubry and Doumer have come to the following conclusions: (1) contrary to the generally accepted opinion, coagulability of the blood in erythraemia is usually less marked than in the normal subject. (2) The number of haematoblasts is generally modified in a remarkable degree, being sometimes much higher and sometimes less than usual. (3) A considerable proportion of the red cells imprisoned in the clot subsequently escape. This phenomenon is not due to fibrinolysis, but is the mechanical result of an abnormal increase in the number of the red cells and of the insufficiency of the fibrin. (4) These changes are not found in erythraemia only, but are present in other forms of polycythaemia. (5) The degree of these changes bears a direct relation to the severity of the polycythaemia. (6) The changes are not the result of hepatic disturbance, but are the direct consequence of an increase in the number of the red cells.

An example of polycythaemia as an hereditary disturbance of internal secretion is reported by Engelking of the Freiburg University Eye Clinic, who describes a family in which polycythaemia had appeared in three generations, the grandmother, mother, and five children, two of whom were boys and three girls, being affected. In addition to signs of polycythaemia the children all showed an infantile build, and the older girls, aged 19 and 15, presented other signs of endocrine disturbance, viz. amenorrhoea, goitre formation, and delayed growth of bones.

Taschenberg, of Munich, reports a case of polycythaemia in a woman aged 58, treated with phenylhydrazin as recommended by Eppinger and Kloss in 1918. In June and July 1919 7·25 gm. were given by mouth, with the result that the number of red cells slightly rose and the haemoglobin fell. After blood-letting the number of red cells fell from 14 millions at the end of August to 6½ millions at the beginning of October. Resumption of phenylhydrazin in smaller doses than before caused not only a very severe anaemia (1,000,000 red cells; haemoglobin 30 per cent.), but also produced a myeloid blood picture. Subsequently, the patient proved refractory to phenylhydrazin. The case shows that this drug is not free of danger, as Eppinger and Kloss declared, though the unfavourable result was not due to large doses, as was shown by comparison with those used by other writers.

Pendergrass gives a brief survey of reported cases of polycythaemia vera and then proceeds to describe a method of X-ray treatment. His aim is to give such a dose that the function of the bone-marrow will be destroyed, and at the same time a stimulating dose to the spleen. He reports a case in which treatment had some slight result. This was very possibly due to insufficient dosage, and it might be well to vary the method by giving actually destructive doses to some bones while leaving others to carry on the supply of a normal number of red cells.

As the result of his experience Böttner, of Königsberg, maintains that X-ray treatment may cure a number of cases of polycythaemia, while in others it has only the effect of symptomatic treatment, though temporarily very effective.

Béclère, who reports two cases, remarks that erythraemia or Vaquez's disease, of which the treatment has hitherto been purely symptomatic, is now amenable to treatment which will produce a complete cure. This treatment consists in Röntgen therapy, but whether the erythraemia is associated with splenomegaly or not the irradiations should be applied to the bone-marrow of the different bones of the skeleton according to the method introduced by Lüdin, of Basle, and not to the spleen. Commenting on Béclère's communication, Vaquez declares that the only chance of recovery in erythraemia as in leukaemia lies in Röntgen therapy, but that no verdict should be given as to the effect of the treatment until six weeks or two months after its application.

For further information on the subject of polycythaemia the recent monograph by Weber (2) should be consulted.

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DIPHTHERIA

Epidemiology. According to Newman, chief medical officer of the Ministry of Health, diphtheria was more prevalent in England and Wales during 1920 than it had been for some years (69,481 notifications and 5,641 deaths). In all areas the notification-rate of 1920 exceeded that of 1919, and, as in the case of scarlet fever, London and Wales were the two worst districts. The interval, however, between London and Wales was much greater than it was with respect to scarlet fever. The London curve began to rise at about the same time of year (June) as that of scarlet fever, and the maximum came in the same week. For several weeks in succession the notification of diphtheria maintained a high level, forming an irregular plateau, and no really important remission occurred. On the other hand, the death-rates appeared to be below those of 1919, and in general the epidemic prevalence was characterized by a low case mortality.

Weaver states that there has been no marked decrease in the diphtheria death-rate in Chicago during the last 20 years. From 1897 to 1906 it was 3·72 per 10,000, and from 1907 to 1916 it was 3·34 per 10,000 of the population. A study of the fatality-rates from diphtheria in Chicago from 1912 to 1919 shows that, while there is a slight fluctuation from year to year, there has been no appreciable decrease in the number of fatal cases, the fatality-rate of 11·31 per cent. for the four years, 1916 to 1919 being almost the same as for the preceding four years, when it was 11·63 per cent. From a study of 147 fatal cases observed in the Durand Hospital, Chicago, during the period 1913–20, Weaver has come to the conclusion that the high death-rate is partly due to neglect by the parents, and partly to inefficient professional care which includes (*a*) failure to cultivate sore throats, (*b*) failure to give antitoxin at once without waiting for the result of the culture, or in the presence of a single negative culture, (*c*) failure to follow patients with a sore throat after seeing them once, (*d*) insufficient doses of antitoxin, (*e*) failure to get the antitoxin quickly in contact with the circulating toxin owing to the employment of subcutaneous injections instead of the intramuscular or intravenous method, (*f*) confusing diphtheria with other conditions such as mumps or quinsy.

Hogan states that the diphtheria death-rate in the city of Baltimore has been remarkably low for the last few years. In 1894 the death-rate from all forms of diphtheria in Baltimore was 15·7 per 100,000. In 1917, 1918, and 1919, it was lower than in any other city with a population over

500,000 with the exception of Los Angeles. The death-rate in Baltimore for these years was 9·75, 11·84, and 13·51 respectively per 100,000 for all forms of diphtheria, and the death-rate at Los Angeles was 7·34, 9·50, and 10·73 per 100,000. 82·11 per cent. of the deaths from diphtheria in Baltimore city during this period were due to the laryngeal form, but as antitoxin was given in only 83·74 per cent., and intubation performed in only half the fatal cases, a reduction in the death-rate might be hoped for by earlier recognition of the disease and timely treatment with antitoxin and intubation.

Vargas, of Barcelona, states that in spite of the progress in the education of the masses, the mortality from diphtheria has increased, so that the numbers of deaths from this cause in Spain, during the year 1919, was 2917, there being 316 cases in January alone, or more than 10 a day. This high mortality he attributes in most cases to negligence, and in some instances to the difficulties of diagnosis.

According to Audouard, diphtheria is endemic among the civilian population of the Palatinate, where it usually assumes a mild form. In the course of 1921, 112 cases occurred in the French army of occupation in that region, most of the cases being found in the artillery and cavalry. Only 5 cases of malignant diphtheria were seen. Several cases of combined diphtheria and Vincent's angina were also observed.

Henry, epidemiologist to the Massachusetts Department of Public Health, Boston, describes an outbreak of 32 cases of diphtheria which were traced to infection of a milk-handler's fingers by *B. diphtheriae*. The incident was interesting in that while neither an outbreak of diphtheria spread by milk nor a true diphtheria wound infection is very uncommon, a combination of both is unique. Another fact of interest was that this wound infection did not give rise to any carriers or clinical cases among fifteen persons at the milk farm, nine of whom were aged from 1 to 20, though the contact had been very intimate.

Symptomatology. The rarity of *diphtheria of the larynx in the adult* is shown by the fact that Rolleston (1) saw only four examples of the kind among 1,156 cases of laryngeal diphtheria with or without faucial involvement admitted to a fever hospital in the course of 16 years, during which period 11,313 diphtheria patients were admitted, 821 of whom were aged 20 years and over. Troisier, Wolf, and Marquézy record two cases of primary diphtheria of the larynx in a man aged 50, and a woman aged 23, admitted to hospital with recession, loss of voice, and paroxysmal attacks of suffocation. Neither had had any previous sore throat or any membrane on the tonsils. After laryngoscopic examination of the man, which showed only oedema of the aryepiglottic folds and vocal cords, an attack of suffocation necessitating tracheotomy ensued and death took place a few minutes after the operation. The autopsy showed membrane extending from the vocal cords to the bifurcation of the trachea. In the second case laryngotomy was performed at once, and 80 c.cm. of diphtheria antitoxin injected. Three hours later tracheotomy was performed. Recovery took place after another 180 c.cm. of antitoxin. Diphtheria bacilli were found in both cases. The writers conclude that in a case of acute primary laryngitis in an adult with recession, attacks of suffocation and affection of the voice the practitioner should always think of diphtheria, and treat the patient accordingly, without waiting for bacteriological confirmation, with large doses of antitoxin intramuscularly and subcutaneously. Laryngoscopic examination is often deceptive, as the supralaryngeal oedema may hide the membrane.

Mallardi, of the Naples Paediatric Clinic, reports a case of *primary anal diphtheria* in a male infant aged 22 months. The anal orifice was red and swollen, and on separating the folds two small fissures were seen covered with membrane. The temperature was 103·6. Recovery took place without complications after two injections of 3,000 units of antitoxin and local application of icthyol.

Bode, of Riga, reports a case of *diphtheria of the glans penis* in a boy aged 6, associated with faucial diphtheria. The disease ran a mild course and no complications ensued. There were two possible modes of infection: (1) direct transfer of the bacilli by the hands to the penis; (2) by the urine. Conradi and Bierast found diphtheria bacilli in the urine of 54 out of 155 cases of diphtheria, and Beyer found the bacilli in the urine of all the 19 cases which he examined.

Cochrane records a case of isolated diphtheria of the penis without any involvement of the throat or nose in a child aged 3, followed by palatal and pharyngeal palsy and squint. Recovery took place.

Atzrott describes a case of *primary diphtheria of the vulva* in a girl aged 11, who infected her brother aged 18 with faucial diphtheria.

Blechmann and Stiassnie relate the case of a boy aged 6½ with a severe attack of diphtheria treated by large doses of antitoxin who developed an extremely painful bilateral *orchi-epididymitis* during the serum rash. As the temperature fell and the other symptoms of the serum disease subsided, the scrotum diminished in size, and the pain disappeared. The writers regard the condition as a hitherto undescribed symptom of the serum disease. A similar case of bilateral orchitis as a manifestation of the serum disease has since been reported by Carrieu, of Montpellier, in a boy aged 13.

At a recent meeting of the Breslau Gynaecological Society, Kühn reported a fatal case of *gangrene and expulsion of the vagina* in diphtheria, of which no previous example has been described. The patient had been admitted to hospital for bilateral adnexitis, and subsequently developed faucial diphtheria. A few days later diphtheritic membrane appeared in the vagina, which became gangrenous and was eliminated with adjacent parts of the bladder and rectum. Bacteriological examination of the gangrenous vagina showed staphylococci and streptococci in the mucous membrane, and diphtheria bacilli in the deeper tissues.

According to Haupt, of the Bonn University Woman's Clinic, who reports a case of *diphtheritic puerperal endometritis* successfully treated by antitoxin, diphtheritic infection of the puerperal uterus is a rare event. This form of puerperal infection was first described by Bumm, who discovered diphtheria bacilli in the membranes of the cervix, vagina, and vulva, in a case of puerperal fever. Unlike faucial diphtheria in which the diagnosis can usually be made from the clinical appearances, the presence of puerperal diphtheria as a rule can only be established bacteriologically, as in the case of wound diphtheria, to which it is closely allied. Lang, of the Giessen University Women's Clinic, who records a case of vaginal diphtheria in the puerperium in a VII-para aged 42, agrees with Haupt that the prognosis of puerperal diphtheria is favourable, provided that a bacteriological diagnosis is made early and followed at once by specific treatment.

Kaiser, of Rochester, N.Y., records a case of *wound diphtheria* which was responsible for an outbreak of diphtheria in a general hospital. The patient was a girl, aged 16, admitted to hospital with the diagnosis of empyema. There was little relief from the operation; repeated small haemorrhages took place through the incision, and the patient presented a picture of toxaemic absorption. On changing the dressings one morning a dirty grey exudate was found about the tubes, from which diphtheria bacilli were cultivated. 18,000 units of antitoxin were injected intravenously, but death from cardiac failure took place a few days later. The necropsy revealed membranous pleurisy and pericarditis. Smears and cultures from the pleural and pericardial membranes and the pericardial fluid showed typical Klebs-Loeffler bacilli. The case gave rise to a laryngeal case and two mild faucial cases among the nurses, three cases in the adult ward, and two cases in children, while throat cultures of 30 children who were negative on admission yielded positive results in 8 cases.

Spieth, of the Ulm Municipal Hospital, records the case of a youth aged 16 with diphtheritic infection of an osteomyelitic wound of the tibia, who subsequently developed faucial diphtheria and infected three other members of the family with faucial diphtheria, to which one succumbed. The case illustrates the danger of diphtheria bacilli in wounds both for the carriers and their environment, as has been shown by Anschütz and Kisskalt, Läwen and Reinhardt, Weinert, and others (vide *Medical Science,* 1919, **1**, 151–2; 408).

Biberstein, of the Breslau University Dermatological Clinic, describes an eczematoid form of *cutaneous diphtheria,* the site of predilection being the ear, on which all stages of acute eczema may be present. The lesions may extend to the occiput, nape of the neck, front of the pinna, neck, and face. The axillary folds, interdigital spaces of the toes, and genitals are also liable to be attacked. The course of the disease is extremely chronic, and there is a remarkable absence of any general disturbance. The local application of the quinine derivatives eucupin and vuzin, proved more effective and economical than serum treatment.

Spiegelberg, who also notes the inefficacy of antitoxin in cutaneous diphtheria, of which he has seen eleven examples in his country practice near Wismar, records a case in which diphtheria of the nape of the neck and umbilicus was followed four months later by motor and sensory paresis of the extremities.

Davidsohn and Heck examined 100 infants for the presence of *diphtheria bacilli in the ears* with the following results. Nine had no discharge from the ear and showed no diphtheria bacilli in the cultures, while all the others had suppurative otitis. In 28 cases or 30·8 per cent. diphtheria bacilli were found. Of these 23 had their virulence tested, and 7 proved to be highly virulent, 2 feebly virulent, and 14 non-virulent. The diphtheria bacilli were never found in pure culture, but always in association with other organisms, especially *B. pyocyaneus* or *proteus*; suppurative organisms such as pneumococci, streptococci, or staphylococci were not found. Although diphtheria bacilli were found to be remarkably frequent in the ear discharges of the children in their institution, the writers are of opinion that these organisms were not the cause of the suppuration, but only a secondary infection, on the following grounds: (1) true middle ear diphtheria is very rare; (2) cases in which diphtheria bacilli were found in the discharge never showed membranous deposit or much destruction of the middle ear, whereas in the more frequently observed diphtheria of the external ear there was always a great tendency to ulceration; (3) the relatively frequent occurrence of non-virulent bacilli; (4) no general symptoms attributable to the toxins of diphtheria bacilli were observed; (5) otitis in which diphtheria bacilli were found did not differ from that in which they were not present. Recovery took place sooner or later under irrigation with formalin. Serum was not employed systematically, as it had proved ineffective in cases with diphtheria bacilli in the nasal discharge. The writers point out that though the infants themselves were not endangered by the presence of diphtheria bacilli in their ear discharge, these organisms were of epidemiological importance in that they might give rise to fresh infections.

Urbantschitsch quotes Jochmann to the effect that diphtheria patients usually lose their bacilli in the third or fourth week of the disease, while in about 15 per cent. they persist to the fifth or sixth or even to the seventh or ninth week. Urbantschitsch records the case of a youth aged 17, who had an attack of diphtheria at the age of 18 months, and of scarlet fever and diphtheria at 3 years, since when he had suffered from bilateral suppurative otitis media. A mastoid operation was performed at the age of 17, and diphtheria bacilli were found in the middle ear on both sides. Meningitis subsequently developed, and the autopsy showed extensive encephalitis without abscess formation. Bacteriological examination of the pus at the base of the brain showed diphtheria bacilli and streptococci.

According to K. Meyer, of the Bacteriological Department of the Rudolph Virchow Hospital, in Berlin, *the occurrence of diphtheria bacilli in the sputum* is by no means rare, although few cases have been recorded in which virulent bacilli have been found. Reye, in 1912, found that in 56 out of 67 cases of diphtheria examined after death, diphtheria bacilli had penetrated into the lungs. In 18 of these cases the diphtheritic sore throat had subsided and death was chiefly due to cardiac complications, and in 12 no anatomical changes were found in the lungs.

Singer, of the Policlinic of the German University of Prague, records a case in a woman, aged 34, suffering from tuberculosis of the hilus glands, in whom examination of the sputum showed a secondary infection with diphtheria bacilli. 2,000 units of diphtheria antitoxin were given, and the sputum, which had been profuse, purulent, and contained a large quantity of diphtheria bacilli, became no longer purulent and showed no more diphtheria bacilli. The toxicity of the bacilli could not be determined, but Singer thinks that they were not completely avirulent, and that they had penetrated the bronchial and hilus glands, where they had given rise to inflammatory changes.

Other cases of pulmonary tuberculosis in which diphtheria bacilli, mostly non-virulent, have been found in the sputum have recently been recorded by Port, of Augsburg, and Lippmann, of Munich.

The rarity of *diphtheria in the first year of life*, and especially of faucial diphtheria, was shown by Rolleston in 1916, who stated that during the fifteen years 1900–1914 the percentage of diphtheria patients admitted to the Metropolitan Asylums Board's hospitals remained fairly constant, varying between 1·5 and 2·8 per cent., while among 2,600 consecutive cases of diphtheria under his care in the course of 12 years, only 20, or less than 1 per cent., were in the first year of life, and of these only 13 had any faucial involvement. Blechmann and Chevalley, after quoting Rolleston's statistics, report a fatal case of faucial and nasal diphtheria in a female infant aged 1 month, who 10 days before the onset of the disease had shown a negative Schick reaction. They conclude that in the infant too much confidence should not be placed in passive immunity of maternal origin, but that the ordinary methods of prophylaxis against diphtheria should be strictly carried out in crèches and nurseries, whether the Schick reaction be employed or not.

Schoedel, of the Chemnitz Obstetrical Clinic, states that diphtheria carriers are frequent among the new-born and in older infants, as is shown by the following statistics recently published by various obstetrical departments relating to the frequency with which diphtheria bacilli were found in the nose of the new-born. Strasburg Midwifery School (Freund), 25 per cent.; Freiburg Women's Clinic (Lembke), 48 per cent.; Giessen Women's Clinic (Kirstein), 84 per cent. At the Chemnitz Obstetrical Clinic, as the result of only two examinations, viz. at birth and on discharge, there were 29 positive results among 49 cases, i. e. in 59 per cent. Examination of 125 older infants showed that 38, or 30 per cent., had diphtheria bacilli in the nose. Repeated examination would probably have shown a higher percentage of positive results. Schoedel concludes that diphtheria bacilli are very frequent in the nose of the new-born, and not much less so in older infants, especially those who live in unfavourable surroundings. Although self-infection is possible, it is not a very frequent event, but it is liable to occur on the supervention of another respiratory infection. Transmission of infection to others is possible, but Schoedel regards the dangers connected with carriers as so slight as to render their notification unnecessary.

Lietz, of the Mayence Midwives' Institute, found that in spite of prophylactic inoculation of mothers and infants, the number of carriers among the new-born continued to be relatively high, and that the number of infants who contracted clinical diphtheria was by no means negligible. He therefore concluded that prophylactic injections were of no value. Since he has substituted the instillation of a drop of a 1 per cent. solution of trypaflavin into the infant's nostrils at birth and for the following 10 days he has had no more cases of nasal diphtheria in the institute.

Brindeau records an outbreak of 9 cases of nasal diphtheria among new-born children in a lying-in hospital. All the children were healthy and born at full term. All but one died in a few days in spite of antitoxin, which was used in five cases. Preventive injections of antitoxin were then given in doses of 5 c.cm., and the epidemic, in which only the infants were affected, was at once brought to an end.

Lönne and Schugt, of the Göttingen University Gynaecological Clinic, examined 300 vaginal smears for diphtheria bacilli from normal pregnant women and from women with various gynaecological affections such as retroflexion, dysmenorrhoea, prolapse, oophoritis, and adnexitis, with a negative result in each case, though in 45 per cent. pseudo-diphtheria bacilli were found. These investigations show that the occurrence of diphtheria bacilli in the vagina is rare and is not an important factor in the infection of the new-born in its passage through the vagina, as some writers assert.

On examination of 242 cases of diphtheria, Smith, of Philadelphia, found that 72 per cent. had no evidence of *cardiac disturbance* apart from an initial tachycardia of 135 to 172, while the remaining 28 per cent., after a lapse of several days in hospital, showed certain vagaries of the pulse, viz. sinus arrhythmia and sino-auricular block in 65 per cent., and premature contractions in 20 per cent., none of these three phenomena being accompanied by symptoms or signs of circulatory embarrassment. The remaining 15 per cent. were cases of high-grade heart-block, which was very sudden in onset and accompanied with urgent cardio-circulatory symptoms with death within 36 hours. Auricular fibrillation was not observed.

Mouriquand, Garnier, and Léorat, of Lyons, record two rare forms of *diphtheritic paralysis*, viz. paralysis of the motor fibres of the hypoglossal and glossopharyngeal nerves in a woman aged 21, and of the facial nerve in a woman aged 20. In the first case the paralysis of the glossopharyngeal and hypoglossal, which was associated with palatal palsy and paresis of the limbs, lasted three weeks. Unilateral paralysis of the glossopharyngeal causing paralysis of one side of the pharyngeal wall does not appear to have been described before in diphtheria. Post-diphtheritic paralysis of the tongue is rare. Only 3 cases were collected by Vernet in his thesis of 1916 (Harris and Henscher, Kender, Körner). Ardisson, in his thesis of 1920, collected another two reported by Sicard and Barbé, and Descos and Vial, and Chauffard and Leconte have also described a case. In facial paralysis, which is less uncommon, sometimes the lower branch only is affected, and sometimes the whole nerve, as in the writers' case. As a rule, facial paralysis in diphtheria is associated with other palsies, such as paralysis of the palate and accommodation, as in the present case.

According to Marie and Mathieu, who record two cases of diphtheritic paralysis in adults presenting the features of paralysis due to spinal cord lesions, the clinical picture in diphtheritic paralysis when there is only a slight intoxication of the nervous system is that characteristic of peripheral neuritis, while, if the intoxication is more intense, groups of cells in the spinal cord become affected, or at least their involvement becomes more obvious, and paralyses indicating a spinal cord lesion are observed.

Powers, of the Neurological Department of the Massachusetts General Hospital, has collected eight cases of disseminated myelitis following diphtheria, including one of his own in a boy aged 10. The picture of disseminated myelitis was complete, but apparently the myelitis did not end in sclerosis, as apart from a suggestion of nystagmus, complete recovery took place. Of the eight cases on record, that reported by Powers was the only one in which antitoxin had been given.

Under the name of the 'doll's eye' (*puppenauge*) Widowitz, of the Graz University Children's Clinic, describes a slight protrusion of the eyeballs with a slow and monotonous movement of the lids due to involvement of the ocular muscles as characteristic of diphtheritic paralysis.

Fromaget, of Bordeaux, reports a case of double optic neuritis in a man aged 32, which developed in association with palatal palsy three weeks after a mild attack of faucial diphtheria not treated by serum. Recovery took place in a fortnight's time under treatment with antitoxin.

De Lavergne and Zoeller examined the blood and cerebrospinal fluid in 11 cases of diphtheritic paralysis with the following results: (1) In most cases of diphtheritic paralysis in adults, antitoxin was present in the blood. This antitoxin is due to a process of active immunization, since it may be found in patients who have not had serum during the acute stage, while in patients who have been treated with serum the antitoxin is still present when the action of the serum would be exhausted (7½ months after its administration), although the antitoxin curve is stationary or rising. (2) In one case in which the patient's serum did not contain any antitoxin, an extremely severe paralysis was present. The writers suggest that the usually mild course of diphtheritic paralysis is due to the blood containing active antitoxin. (3) As a rule, no trace of toxin or antitoxin was found in the cerebrospinal fluid of cases of diphtheritic paralysis.

Numerous French writers such as Haguenau, Hallez, Kapetis, and Merklen, Weiss, and De Gennes have recently emphasized the frequency of a meningeal reaction in diphtheritic paralysis. Kapetis, in his Paris thesis, has collected 17 cases, including one not hitherto published of diphtheritic paralysis in which lumbar puncture was performed and chemical and cytological changes were found in the cerebrospinal fluid. In 16 cases there was an excess of albumin ranging from 3·25 gm. to 0·40 gm., the lymphocytosis varying from 30 to 5 per cubic millimetre. The cerebrospinal tension was increased in six cases, normal in nine, and in three was not examined. In nine cases there was an albumino-cytological dissociation, i. e. the excess of albumin was accompanied by a normal cell count. These meningeal reactions were observed both in severe and in mild cases, and were still present at the time of clinical recovery. Dissociation between the amount of albumin and the cellular content of the cerebrospinal fluid is attributed by Kapetis either to the vascular congestion which is seen *post mortem* in cases of diphtheritic paralysis or to a modification in the permeability of the meninges following affection of the choroid plexuses. Hallez compares the meningeal reaction in diphtheritic paralysis to that met with in various intoxications, as demonstrated by Mosny and Malloizel in alcoholism and by Widal in uraemia.

The *association of diphtheria and syphilis* is illustrated by Friedemann, director of the department for infectious diseases of the Rudolph Virchow Hospital in Berlin, who, during the last six years has seen ten cases of diphtheria in which the membrane remained unchanged after a fortnight's treatment. In two cases it persisted for over 15 and 18 months respectively. In all the cases the connexion between syphilis and this chronic form of diphtheria was proved by a positive Wassermann reaction and the prompt effect of antisyphilitic treatment. The comparative rarity of chronic diphtheria in spite of the frequency of diphtheria and syphilis is attributed to syphilis being mainly a disease of adult life and to diphtheria principally affecting children. Some unknown constitutional factors may also possibly play a part in the causation of chronic diphtheria.

Flurian reports a case in an infant, aged 1½ months, in whom an attack of severe faucial and nasal diphtheria awakened a hitherto dormant congenital syphilis. Recovery took place under specific treatment.

Prophylaxis. Garland reports on a Schick test campaign undertaken by him in 14 of the larger cities of the state of Massachusetts. 380 tests were carried out in 16 hospitals. In most cases the tests were performed on nurses, hospital employees, and physicians. 52·8 per cent. were found to be susceptible to diphtheria, a much higher percentage than Park found in his adult group (12 per cent.). Garland regards this result as an indication that there is a greater susceptibility to diphtheria among the educated classes than had previously been supposed. The experience of Zingher (1), of New York, Fleischner and Shaw, of San Francisco, and O'Brien and his collaborators was similar. During a diphtheria outbreak in a private school of 150 students, Fleischner and Shaw found 65 per cent. of the Schick reactions positive among boys aged from 8 to 18 years of age. Zingher, from his experience of the Schick test and the control test in more than

52,000 school children in 44 public schools in two New York boroughs, found that the children of the well-to-do classes had a much higher proportion of positive Schick reactions than the children of the lower classes, and attributed this to the relative segregation of the former and the close contact of the latter. He also noticed that the factors of race and hereditary family tendency seemed to influence considerably the development of natural immunity to diphtheria. Thus children of the coloured race, in spite of the crowded condition in which they lived, showed a high proportion of positive reactions, while the lowest percentage of positive reactions was given by children of Italian extraction living in the crowded East Harlem section of New York City. Children of Hebrew parents varied considerably in the percentage of positive reactions. Those living in the congested districts gave a low percentage, while those living in the upper west side of the city were among those who gave the highest percentage of positive reactions. The importance of the family factor was shown by there being a marked tendency for all the children of the same family to give a similar Schick reaction whether positive or negative (Armand-Delille and Marie had had a similar experience, vide *Medical Science*, 1921, **4**, 26. J. D. R.)

O'Brien, Okell, Glenny, and Baxter, carried out 1,150 Schick tests with the following results: (1) In a group of medical students only 56 gave a negative reaction, in other words, there was a low immunity of 35 per cent.; (2) of 22 nurses in the same institution only 45 per cent. were immune; (3) in a hospital staff of 182 adults consisting of doctors, nurses, and attendants, 78 per cent. were immune; (4) in a group of 734 children in an institution where diphtheria had recently occurred, 534, or 73 per cent., were immune; (5) it was generally found that brothers and sisters gave the same reaction.

Muslow, of the John McCormick Institute for Infectious Diseases, Chicago, carried out the Schick test on 97 nurses, of whom 65, or about 67 per cent., gave a positive reaction, and on 40 medical students of whom 27, or 66 per cent., were positive. Approximately 75 per cent. of those with a positive reaction became negative after injection of toxin-antitoxin. Injection of antitoxin soon after the administration of toxin-antitoxin seemed to interfere somewhat with the effect of the latter. It was found that severe reactions to injections of toxin-antitoxin in hypersensitive persons or those having a persistently positive Schick reaction could be avoided by injecting smaller amounts without interfering with the development of immunity.

Flamini investigated the Schick reaction in a foundling hospital at Rome in 145 infants at the breast, 190 nursing women, and 125 weaned children aged from 1 to 3 years. Infants from 3 to 4 months of age gave a positive reaction in 17 per cent., from 4 to 8 months in 29 per cent., from 8 to 12 months in 39 per cent., during the second year in 46 per cent., and in the third year in 50 per cent. These figures correspond fairly closely with those of Park as regards infants in the first few months of life, and less as regards the age from 6 to 12 months, a period at which, according to Park, the percentage rises to 60. The ages of the nursing women ranged from 17 to 30, most being about 20. Positive reactions were obtained in 60, or about 32 per cent., and negative in 130. No relation was found between the mother and child or between the nurse and the suckling as regards the presence or absence of antitoxin, the infants' immunity not being inherited nor conveyed through the milk.

Other recent statistics relating to the Schick test will be found in the articles by Copeman (1) (2), Dickinson, and Ward, in this country, and by Armand-Delille and Marie, Lereboullet and Marie, Marcais and Méry, Guinon and Marie, in France.

Park (1), of New York, discusses the question whether a negative Schick test indicates present or future security from diphtheria. During the past 8 years he has collected 18 cases of suspected diphtheria occurring in children who had given a negative Schick test; 6 of these he regards as due to errors. Comparing the Schick test with vaccination, he points out that a positive Schick test or a successful vaccination is a definite sign of a lack of immunity, whereas a negative Schick reaction or a negative result from vaccination is a strong suggestion of immunity, but not an absolute assurance.

From observations on 260 children who had been injected with toxin-antitoxin, J. Meyer, of New York, found that the duration of immunity conferred thereby, as determined by the Schick test, was 44 months in 94·4 per cent. of the cases, 20 months in 83·5 per cent., and 16 months and 5 months in 97·5 per cent.

According to Zingher (2), two injections of toxin-antitoxin, even when a large dose is used, do not give such good results as three injections of a smaller amount. He advises that children under six months of age should not be given toxin-antitoxin, as in 85 to 90 per cent. they are immune and do not respond to the injections, as is shown when a Schick test is performed later. On the other hand, all children from six months to five years of age should be given toxin-antitoxin. Omission of the Schick test is not of much consequence in this group as most of the children at this age give a positive reaction.

102 children who gave a positive Schick reaction were immunized by O'Brien with three separate inoculations of toxin-antitoxin at intervals of about a week between each injection. Slight local reactions were common, but practically no general reactions occurred. On the other hand, though children practically never develop severe reactions, O'Brien and his collaborators state that great caution is required in carrying out active immunization in adults. They quote the case of a doctor subject to migraine and very sensitive to serum, who gave a marked early reaction to the Schick control and suffered severe local pain and malaise from the first injection of 0·01 c.cm., and the second injection of 0·02 c.cm., whereas initial doses of 0·05 c.cm. and even 1 c.cm. had not caused any discomfort in children.

Blauner reports eight cases of diphtheria which occurred among children who had been immunized by three doses of toxin-antitoxin. Park (2), commenting on these cases, makes the following suggestions: (1) The amount of antitoxin as shown by the negative Schick reaction had been insufficient to prevent a moderate attack of diphtheria; (2) some other infection had caused the croupous tonsillitis, and the diphtheria bacilli were accidentally present in carriers; (3) the sore throat started by the pyogenic organisms had paved the way for the local action of the accompanying diphtheria bacilli.

White, director of the Biologic Laboratories in the Massachusetts Department of Public Health, states that under no circumstances should the mere fact that a person has received the usual course of toxin-antitoxin be relied upon as proof of complete protection against diphtheria. He recommends that all immunizations should be controlled by subsequent

Schick tests and that all persons with a positive reaction should be given a second course of injections of toxin-antitoxin.

Treatment. Greuel, of the Hamburg-Eppendorf Hospital, records two cases, one of laryngeal diphtheria in a child aged 8, and the other of severe faucial diphtheria in a woman aged 32, resuscitated by intracardiac injection of adrenalin after life was almost extinct. In the first case a single injection of 1 c.cm. of adrenalin was given, and in the second three intracardiac injections of adrenalin and 1 c.cm. of extract of the posterior lobe of the hypophysis were followed by intramuscular injection of caffein and camphor and intravenous injection of glucose.

Bie's investigations at the Blegdam Fever Hospital concern: (1) the effect of serum on the temperature; (2) the ability of serum to prevent the extension of the false membrane; (3) the ability of serum to hasten the disappearance of this membrane. A comparison of the temperature curves of cases treated and not treated with serum showed that this had no effect on the course of the fever. Even when the serum was given by intravenous injection it had no effect on the fever. The ability of serum to prevent the extension of the membrane cannot be accurately gauged, as the disease at present is less severe in this respect than in the 'eighties. As for the third point, Bie's figures suggest that serum may help to hasten the disappearance of the membrane, but this process depends mainly on the patient's own reactive powers. And whether the serum was given in small doses or large, by intravenous, subcutaneous, or intramuscular injection, the result in this respect was the same.

Turning from these rather negative merits of serum to its effect on the actual mortality of diphtheria, and the influence of large doses of serum on this mortality, Bie shows that the increasing dosage adopted at his hospital can be correlated with a decreasing mortality. To reduce the dangers of introducing large quantities of foreign protein and carbolic acid into the body, the State Serum Institute in Denmark has, since January 1921, provided for intravenous injection a serum containing 1,400 units per c.cm. instead of only 400 units per c.cm. as heretofore. Bie has not been able to detect an appreciable increase in the frequency and severity of serum disease in connexion with his increased dosage, but this leads to more frequent occurrence of oedema, notably at the site of injection and in the upper lip. The largest single dose he has yet given was one of 196,000 units (28,000 intravenous, 168,000 intramuscular) to a woman of 32. The largest total dose was 350,000 units, of which 56,000 were given intravenously. The greatest total quantity of serum yet given was 850 c.cm., the patient being a girl of 10. A comparison of the diphtheria mortality in different years showed that by abandoning small and moderate doses of serum in favour of enormous doses the mortality in 1920 and the first two months of 1921 was less than a third of that of the average mortality in 1896, 1900, 1908, and 1915. The routine at present adopted by Bie is to give an intramuscular injection in every case, and to supplement it with an intravenous injection on the patient's admission if the condition is alarming. The same or a smaller dose is given next day, and daily injections are repeated till the local condition is regressive.

Aviragnet, Lereboullet, and Marie have employed the following method to show the inefficacy of antitoxin when given by the digestive tract as recommended by Dufour, of Fécamp. Nine children aged from 3 to 10 years, with a positive Schick reaction, were given by mouth, in the course of 1 to

3 days, 20 c.cm. of antitoxin containing 250 units per c.cm., and then had their reaction tested again. Contrary to what occurs after a subcutaneous injection of antitoxin, which makes a positive reaction negative, in none of the cases did the ingestion of serum have the least effect on the intensity of the reaction. The same result was obtained in 6 children after injection of 20–40 c.cm. of antitoxin into the rectum. Raymond, of Lyons, also used the same method to prove that the rectal mucous membrane absorbed little, if any, antitoxin.

The prevention of the serum disease both in diphtheria and tetanus by the employment of immune ox serum instead of horse serum is recommended by Kraus, director of the Butantan Serum Institute at São Paulo, who, alludes to his previous paper written in collaboration with Cuenca and Sordelli, of the Buenos Aires Department of Hygiene, in which they showed that serum manifestations were much rarer after the use of immune ox serum than after immune horse serum in the prophylaxis and treatment of diphtheria and tetanus.

Dujarric de la Rivière has treated 50 carriers by hot air, an ordinary electric dryer with a sterilizable mouthpiece 5 cm. long being employed. Before insufflation the patient's lips should be smeared with vaseline. The apparatus should be placed so that the extremity of the mouthpiece should be on a level with the buccal orifice. It is not necessary to bring it nearer to the nostrils. A wooden tongue depressor is used by the patient and the jet of hot air is directed towards the points in which diphtheria bacilli are usually most abundant. The treatment should last 10–15 minutes at a time, with intervals of half a minute in which the apparatus is withdrawn. The number of sittings needed to free the throat of bacilli varied between 3 and 5. In only one case were as many as 15 needed. The treatment is without danger, the mucous membranes tolerate the hot air very well, and no burns were seen. The method is readily applicable in adults, but in children it may be very difficult or even impossible on account of a spasm of the throat concealing the tonsils.

Audouard, who approves of this method, advises the following treatment of healthy carriers and convalescents : (1) Two applications of hot air in the course of 24 hours from 5 to 10 minutes according to the patient, the mouthpiece being held at a distance of 8 cm. from the lips ; (2) insufflations of antimicrobic serum every evening to the nasal fossae and nasopharynx on which the hot air does not act.

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J. D. R.
C. L.

ABSTRACTS

SURGERY

Levy, A. G. Chloroform anaesthesia. *London: John Bale, Sons & Danielsson.* pp. viii + 159.

Dr. Levy has written an interesting book on an old subject. His experience both as an anaesthetist and as a laboratory worker has enabled him to deal with his subject in a manner denied to others, for in this book he carries the results of laboratory experiment to the practising anaesthetist, and makes clear to the academic worker the difficulties of the anaesthetist and points out certain gaps in our knowledge.

Dr. Levy is well known for his researches on chloroform syncope, the proof of the importance of ventricular fibrillation in this connexion, and the determination of the factors which favour the onset of this condition under chloroform. His research work necessitated, amongst other things, an exact analysis of the action of chloroform on animals; and we are given the results of this, in addition to his own work, in the first part of this book. This is followed successively by a consideration of the application of the established facts to the administration of chloroform to man; deaths under chloroform and their prevention; apparatus used by anaesthetists and their defects; clinical considerations; and finally delayed chloroform poisoning. The work is well done and the subject-matter clearly expressed. Within the limits allowed a full discussion of debatable points cannot be expected, but the summaries are usually judicious. Possibly considerations of space prevented the inclusion of sections dealing with the capillary circulation, the relationship of chloroform to shock, and other after-effects, in addition to delayed chloroform poisoning, which is, fortunately, a rare condition in man.

There is evidence of hurried proof-reading, as minor mistakes on pp. 45, 67, 100, and 128 show. On page 106 a more serious error occurs. Intermittent cardiac massage is recommended for restoration of the heart-beat when ventricular fibrillation has developed, and the following statement is made. '. . . pauses should be allowed at intervals, these pauses varying from fifteen up to sixty *minutes* in duration.' Clearly seconds should be read for minutes, but a mistake of this kind in this particular section should not have been allowed to pass.

A good bibliography is included at the end of the book.

P. P. L.

Panner, H. I. Ejendommelig Lidelse i Capitulum ossis metatarsi. [**A characteristic disease of the heads of the metatarsal bones.**] *Hosp.-Tid.*, **1922, 65,** 6–9.

During the past two years Panner has observed 10 cases, and his colleagues have provided him with records of three other cases, of a disease with well-defined characteristics. Of the 13 patients, 3 were adults, and of the 10 children, 9 were between the ages 10 and 14. There was no evidence of any constitutional disease such as tuberculosis or syphilis, and the onset was spontaneous and insidious, a history of trauma being obtainable only in one case. The first symptom was pain on walking, the second metatarso-phalangeal joint being the seat of the pain in all but one of the cases. In this case the third metatarso-phalangeal joint was affected. The pain was seldom severe and was never felt at rest. A definite, but not large, swelling, most marked on the dorsal aspect of the foot, was demonstrable over the joint, which was usually very tender on pressure. But there was never any heat or redness of the skin. There was only slight limitation of movement; as a rule, plantar flexion was somewhat reduced, and extreme passive movement was somewhat painful. In two cases lateral movements were very painful. The disease tended to heal spontaneously without leaving much limitation of movement apart from a slight reduction in the range of plantar flexion. No radical treatment proved necessary, and protecting the foot from overstrain was sufficient.

The primary lesion is situated in the head of the metatarsal bone, and the X-rays show flattening of its articular surface and shortening of the head of the bone in the long axis. There are ill-defined shadows at the place where ossification begins in the epiphysis, and alternating with these shadows there are irregular, comparatively translucent patches. The outline of the joint is well defined, but has a somewhat irregular contour, showing in many cases an outward bulge in the middle. The diaphysis of the bone is never affected early in the disease, but in rare cases, and late in the disease, it may become thickened by periosteal deposits, the distal half of the bone showing a uniform enlargement. Synostosis often occurs earlier between epiphysis and diaphysis on the diseased than on the healthy side. With regard to aetiology, the disease must be distinguished from simple arthritis deformans provoked by numerous slight injuries, for the X-ray picture is quite different. The suggestion that an undetected fracture of the bone is responsible for all the symptoms and X-ray changes, can also be dismissed as unlikely, and it is certain that the disease belongs to that group which the X-rays have shown to be benign disorders of growth. Among these are Calvé-Perthes's hip disease, Köhler's disease of the os naviculae pedis, Schlatter's disease of the tuberosity of the tibia, and Scheuermann's disease of the spine (*Medical Science*, 1920, **2**, 461).

C. L.

DEUTSCHLÄNDER, C. Über eine eigenartige Mittelfusserkrankung. [**On a peculiar disease of the metatarsus.**] *Zentralbl. f. Chir.*, 1921, **48**, 1422.

Deutschländer describes a disease of the metatarsus that he regards as new and that, in typical cases, affects the second and/or the third metatarsal bones, in the distal third of the diaphysis at its junction with the middle third. He has seen six cases, all in women about 30 years old ; the onset was spontaneous, no history of strain or other injury being obtainable. During its course the disease passed gradually through three stages, each lasting two or three months. During the first period the patient complained of pain in a definitely outlined area, but physical examination and radiograms revealed nothing. Later the pain diminished and radiography showed thickening of the bone both in the medullary and periosteal aspects.

In the third stage the new bone thickening disappears and there is gradual restoration to the normal appearance.

The author considers the condition to be one of subacute osteitis and periostitis due to an attack, through the nutrient artery, by attenuated bacteria. Köhler has described a condition in the second metatarso-phalangeal joint of the nature of an osteochondritis, but this may be distinguished from Deutschländer's disease, according to the latter author, by the fact that in the disease under review the changes take place in a very definite area of the bone shaft; this localization also seems to distinguish it from the late rickety changes at the metaphysis, described by Fromme. Treatment consisted in firm bandaging, combined with passive hyperaemia.

This paper by Deutschländer and the one by Panner, abstracted above, suggest that some of the cases, clinically diagnosed as Morton's disease, may in reality be associated with the underlying radiographically visible changes described by these two writers or with those described by Fromme or by Köhler in connexion with the second metatarsal.

C. C. C.

Rud, H. Om Fibro-adenoma mammae hos Mænd. [**Fibro-adenoma mammae in men.**] *Hosp.-Tid.*, 1922, **65**, 253–66, 269–74.

In addition to recording in detail 5 cases of fibro-adenoma in men between the ages 18 and 22, Rud reviews the literature of tumours of the breasts in males, and notes that in men, as well as in women, malignant growths are far more common than benign growths. In four of his cases there was a history of trauma, single or repeated, dating back 3 weeks to 8 months. The conclusions to which he comes are the following: a tumour having been found in the breast, the patient must not be lost sight of till the tumour has been removed. If there are signs of mastitis, the treatment should be conservative as long as the mastitis lasts. But when redness and tenderness have disappeared, and the tumour, which may at first have been diffuse, has become better defined, it should be removed, both because it has not disappeared spontaneously and because it is likely to grow—slowly perhaps—and to cause pain and to interfere with the patient's work. A third cogent reason for removal is the prospect of the advent of malignant disease. In doubtful cases it is unwise to rely on the findings of an exploratory excision; it is wiser to amputate the breast at once and to extend the operation to the axilla, for even though the sample examined after the exploratory excision may seem benign, other parts of the tumour may contain malignant elements. But, as a rule, it is sufficient to excise the tumour alone, and, as fibro-adenomata are usually well defined, their removal is easy. If they are not well defined, all the breast structures must be removed.

C. L.

Perman, E. Haematoma in the sheath of the musculus rectus abdominis. *Acta Chir. Scand.*, 1922, **54**, 434–54.

Perman, who records in detail 11 cases observed by himself, and abstracts 9 others from the literature, points out that though haematoma in the sheath of the rectus abdominis muscle is usually dismissed in a few lines in surgical text-books, it is a common condition presenting many interesting features. The assumption that the diagnosis is easy requires revision. 17 of the 20 cases were operated on, but only in 6 was the right diagnosis made or suspected before operation. Only in 3 cases was a positive diagnosis made at the first examination in hospital. In no fewer than 6 cases torsion of an ovarian cyst was diagnosed or suspected. In 3 cases the hypothetical ovarian cyst was distinctly felt through the vagina, the large haematoma in the lower part of the rectus sheath bulging into the abdominal cavity. Other mistaken diagnoses were intestinal obstruction (1 case), ruptured extra-uterine pregnancy (1 case), appendicitis (several cases) incarcerated hernia in the abdominal wall (1 case), tumour of the abdominal wall (2 cases). Other conditions with which this haematoma is apt to be confused are gummata, tuberculosis, and actinomycosis of the abdominal wall.

Two chief reasons account for the frequency with which such mistakes are made. The signs and symptoms mimic very closely those of other conditions, and the surgeon is apt to rely on a history of strain and an acute onset for his diagnosis. As a history of strain (lifting, coughing, and the like) is often lacking, and as the onset of the condition is often insidious, the clinical picture does not tally with some surgeons' preconceived notions about this accident. The haematoma is usually found between the umbilicus and the symphysis, and as a rule only one rectus is involved; in only one of Perman's 11 cases was the lesion bilateral. The remaining 10 cases were equally distributed on the two sides of the body. His first case was that of a recruit who was learning to ride and to mount without the help of stirrups. Within five days of joining his regiment he felt pain in the lower abdomen. Exploratory incision of the abdominal wall revealed a haematoma in the sheath of the rectus. Evacuation and primary suture were followed by healing by first intention. With regard to treatment, operative evacuation is indicated when the haematoma is so large that its spontaneous absorption would take a comparatively long time, and when it is infected. This is often the case when the haematoma develops during an attack of typhoid fever, influenza, or other acute disease. Evacuation of a non-septic case should be followed by primary suture. Perman adds that rupture and haematoma of the lateral abdominal muscles are exceedingly rare. C. L.

LUNDBERG, S. Retrograde Dünndarminvagination nach Gastro-enterostomie. **[Retrograde intussusception of the small intestine after gastro-enterostomy.]** **[B.]** *Acta Chir. Scand.*, 1922, **54**, 423–33.

In a paper on retrograde invagination of the upper section of the jejunum, Lundberg records one case observed by himself, and reviews the records of eight similar cases in which, some considerable time after an anterior or posterior gastro-enterostomy, retrograde invagination occurred. His own patient was a married woman, aged 41, on whom, on November 16, 1911, resection of the pylorus and anterio-gastro-enterostomy and entero-anastomosis with Murphy's button was performed. She was readmitted to hospital on January 21, 1921, with signs of acute intestinal obstruction. The correct diagnosis was not made during life, and she was too debilitated on admission to hospital to undergo an operation. The afferent coil of jejunum was found at the necropsy to have undergone retrograde invagination for a distance of 20 cm. Most of it was gangrenous, and the stomach and adjacent coils of gut contained blood-stained fluid. The rest of the gut was empty, and there was no sign of peritonitis. There was also no sign of cancer of the stomach, although this had been diagnosed at the operation in 1911.

The other cases are those published by Steber, Baumann (two attacks in the same patient), Hatert, Schloessman, Amberger, and Eberle (two cases). These show that the gastro-enterostomy opening allows of retrograde invagination more readily than the pylorus. It is possible that the increased rate at which food traverses the stomach after gastro-enterostomy entails abnormal irritation of the small intestine, which may contract more powerfully than under ordinary conditions. The clinical picture is well defined, but the only case in which the diagnosis was made before operation or death was Baumann's, and he had the peculiar advantage of the record of the same accident at an earlier date in the same patient. The onset is acute, and the violent colic in the epigastrium is incessant and is associated with vomiting. In five cases the vomit was blood-stained, and in one case it was faecal. There is seldom any appreciable rise of temperature, and distension of the abdomen is an inconstant sign. As a rule, there is tenderness with rigidity in the epigastric or umbilical region, the rest of the abdomen being flaccid and not tender. But in Amberger's case the whole of the abdomen was distended and tender. Recovery has followed in all the cases hitherto operated on, the interval between the accident and the operation being 18 hours to 4 days. In the 4-day case it is doubtful whether the invagination had lasted all this time. The 2 patients not operated on died within 4 days. C. L.

Albo, M. Hydatid cysts of the pancreas. *Surg. Gynec. & Obst.*, 1922, **34**, 739.

Although hydatid cysts are relatively common in different parts of the body they are of extreme rarity in the substance of the pancreas. Albo, in his present communication, has carefully analysed the reported statistics and shows that there is only an incidence of 0·12 per cent. among the total number of hydatid cysts. Another series of collected figures shows that the pancreas is not affected.

An account is given of the life-history of the *Taenia echinococcus* and a discussion follows as to the possible methods of entry. Most commonly they come from the intestines through the portal circulation, and this explains the greater frequency of liver infections. Another possibility is that the larvae pass through the lymphatics to the general venous system and hence make their way to the lungs. The possibility of infection by inhalation, the author says, may be disregarded. As regards the pancreas, infection is probably always through the blood-stream. There appears to be little or no evidence of direct migration up the ducts from the duodenum. The changes, once the embryo has reached the pancreas, are identical with those elsewhere in the body, but the cyst as it develops tends to become subserous and thus may project in any one of the positions taken up by other cysts of the pancreas. Clinically cysts in this region may be divided into three groups: (1) Those which develop in a latent or almost latent manner and give rise to a palpable tumour. (2) Those which develop rapidly, producing symptoms resembling carcinoma of the bile-ducts or of the head of the pancreas. (3) Those which produce symptoms resembling retroperitoneal tumours.

A detailed description is given of the methods of diagnosis, commencing with a differentiation of tumours of the abdominal wall from intra-abdominal tumours and passing on to the differentiation of other retroperitoneal tumours. It is interesting to note that in the distinction of one cyst from another he states that neither eosinophilia nor deviation of complement are constant findings, and that the tumours are almost if not entirely immobile. (Cysts of the pancreas are, however, frequently mobile, although the reverse is stated in nearly all monographs. The normal pancreas has a very considerable range of movement and in thin patients can be freely palpated and moved. Small cysts and tumours of the pancreas can be readily displaced for two to three inches in either direction and the movement will be correspondingly increased if the patient has general ptosis. It is only when the cyst or tumour becomes very large that it becomes fixed in the same way as any other retroperitoneal tumour.)

In discussing the treatment he shows that no drugs are of any value, and therefore operation should be carried out. Only in very early cases is extirpation possible. In others the cyst should be carefully isolated from the general peritoneal cavity to prevent dissemination. He advocates evacuation of the cyst and then the injection of a parasiticidal fluid, preferably a 2 per cent. solution of formaldehyde.

A list of reported cases is given both from autopsies and operations. Fifteen operated cases are described, including one case of the author's.

A. J. W.

Primrose, A. Pancreatic cysts and pseudocysts. *Surg. Gynec. & Obst.*, 1922, **34**, 431.

The author makes use of the classification suggested by Mayo Robson and Moynihan in 1903, adding only to this list dermoid cysts, since one was reported by Judd. He regards acute and chronic pancreatitis and also infections of the gall-bladder and bile-ducts as important aetiological factors. He points out that there is still some confusion as regards the treatment of the biliary apparatus in cases of pancreatitis. On the one hand, Judd advocates cholecystectomy in the belief that the intrahepatic pressure will rise until it overcomes the obstruction of the sphincter. On the other hand, McWhorter points out that such a rise of pressure may force the bile along the pancreatic ducts and hence increase the condition. In view of these diverse findings Archibald has advocated prolonged drainage of the common bile-duct. (This difficulty has been realized for some time and the most satisfactory solution seems to be to remove the gall-bladder if it is grossly diseased, always following this step by dilatation of the sphincter through the common bile-duct, or, if this is insufficient, by the formation of a new bile-duct. If the gall-bladder be only slightly diseased the most satisfactory results will appear to follow a cholecystenterostomy).

The author points out that many cysts may follow trauma, but he does not appear here to draw a sharp distinction between true and pseudo-pancreatic cysts, although later he lays stress upon the confusion that exists in the literature between these two conditions. In distinguishing between the two lesions neither the presence of an epithelial lined membrane nor pancreatic ferments are clear indications of the origin of the cyst, for ferments may be present with pseudo-cysts and the epithelial lining may be absent with true cysts. Reliance has chiefly to be placed upon the anatomical relationship of the cyst-wall.

He reports in detail the case of a large pancreatic cyst which was accidentally found in a woman immediately after pregnancy. The cyst was large and extended down into the pelvis and was mistaken for an ovarian cyst. By careful dissection the cyst was found to be attached to the tail of the pancreas; the pedicle was ligatured and the cyst removed. Although it contained some 5 litres of pale, chocolate-coloured fluid, its anatomical relationship would seem to show that it was a true and not a pseudo-cyst.

Several cases are quoted from the literature in which complete extirpation has been successfully accomplished. A. J. W.

Tenani, O. Contributo alla chirurgia della papilla del Vater. [**Contribution to the surgery of the papilla of Vater.**] *Policlin.*, 1922, **30**, Sez. Chir., 291.

The author's case resembles the hitherto unique experience of Kausch. A soldier, aged 33, suffered for a year from gastralgia and anorexia, with slight recrudescent jaundice, general weakness, nausea, and loss of flesh. Abdominal walls atonic; lower margin of liver visible two fingers-breadth below the costal margin in inspiration, with a pear-shaped mass to the right of the umbilicus. The liver was hard and the edge defined; the mass hard, tense, irregular in outline, smooth, and tender; lower margin of stomach two fingers-breadth above the pubes; splenic dullness increased; no free fluid; pain at the epigastrium. Diminution of trypsin and steapsin. Diarrhoea; no bile in faeces; crystals of fatty acids; undigested muscle; traces of blood. Glycosuria 3 per cent. Anaemia with lymphocytosis.

The first operation disclosed great dilatation of the whole biliary tract. Duodenotomy revealed a mass the size of a 'nut' obstructing the mouth of the ducts, and two smaller bean-size nodules in the inter-duodeno-pancreatic tissue.

Gastro-enterostomy and choledochenterostomy were performed. One month later resection of the second part of the duodenum was done; the pancreas was crushed and divided in corresponding line so that the whole head was removed with the duodenum; control of the distal end of the body of the pancreas was secured by mattress suture, avoiding the main duct; implantation *en masse* into jejunum was then performed. After a long period of extremely severe shock, which required two blood transfusions in the first six days, recovery followed.

Blood and other abnormal constituents were present in the faeces for twenty days, but then disappeared. Traces of glycosuria were found even after three months; recovery was complete in four months, and health and strength was retained after three years.

The growth was a carcinoma with cylindrical and goblet cells; there were no cubical cells, and the origin was therefore probably from duodenal mucosa; lymph glands showed no invasion, but some inflammatory reaction.

In considering the pathological anatomy of such tumours, distinction must be made between the ampulla and the papilla. In the former three epithelia meet; those of the bile-duct, of Wirsung's duct, and of the duodenum. The papilla or caruncula major is by no means always present and the formation of the ampulla varies widely, so that the two ducts may open separately or together—separated by a mere spur—or into a sort of antechamber—the true ampulla. Moreover, tumours of the lower portion of the common duct, or of the pancreatic tissue proper, may reach the situation of those arising actually in the ampulla. Histological proof, too, is difficult, since the epithelium of the ampulla resembles that of the duodenum. Tumours arising within the muscular walls of the duodenum, as those of the ampulla should, are extremely rare. Ferrari found nine cases among 3,218 carcinomas; Kehr three cases among 2,000 operations on the biliary tract. The tumours are small and hard, and easily mistaken for an impacted calculus; in the rarest instances there is but an ulcerated plaque; the epithelium is cylindrical with goblet cells, whilst those from the pancreatic duct are cubical-celled.

These tumours may be long unsuspected, and their signs, when they do arise, are those of mechanical obstruction. The whole biliary tract is enormously distended, the only differentiating point being that calculi are much rarer than in growths of the tract itself. The jaundice is said to be 'oscillating' rather than intermittent. The presence of blood in the faeces is, perhaps, the one sign suggestive of ampullary tumour as distinct from other tumours and impacted calculus. Suppression of pancreatic function tends to be extreme.

The pancreas rarely suffers metastasis and is seldom invaded directly. The lymphatic arrangement suggests that the liver should be most liable to metastases, but even these are rare.

The course of the disease is steady and the duration perhaps a year.

E. R. C.

Reel, P. J., and **Burrell, N. E.** **Cystic dilatation of the common bile duct.** *Ann. Surg.*, 1922, **75**, 191.

The authors state that the literature records but thirty-six cases of cyst of the common bile-duct. They say that the term cyst does not adequately convey the nature of the pathology, and that the lesion is, in all probability, a diverticulum of the duct.

A review of the reported cases indicates that some of them may have involved biliary passages other than the common bile-duct. They report at length a case of a woman, aged 56, who had had a steadily increasing swelling in the epigastrium for thirty-six years. For eight years there had been a more rapid increase in size with pain and intermittent jaundice. The abdomen was more distended than with a full-time pregnancy, the distension being due to a fixed mass which exhibited fluctuation. An operation revealed an enormous cyst which during exploration ruptured and allowed the escape of 8 litres of thin greenish-yellow fluid. The cyst was drained. Convalescence was uneventful, the wound healing at the end of three weeks. A piece of excised cyst-wall showed occasional areas of liver substance.

The authors mention as possible causes of such cysts the presence of valvular obstruction or congenital obstruction. In discussing the treatment they say that an investigation of the reported cases would seem to indicate that drainage is insufficient. Of thirty-two cases so treated in the literature twenty-one died. Of eight cases of choledochenterostomy five recovered, in two the operation being primary and in three being performed at the second stage. Extirpation was fatal in all three of the reported cases.

A. J. W.

Hartman, F. L., Smyth, C. M., and **Wood, J. K. Results of high ligation of the cystic duct in cholecystectomy.** *Ann. Surg.*, 1922, **75**, 203.

The authors discuss the physiology of the normal gall-bladder, and the various views that have been put forward in the literature are mentioned. They themselves are of the opinion that the gall-bladder has a definite function in storing the bile and in regulating its flow. They were, therefore, in doubt as to what happens to the stump of the cystic duct after removal of the gall-bladder and high ligation of the duct. A series of experiments were carried out on dogs—the cystic duct being ligatured and divided close to the gall-bladder, the stump that was left varying in size from 6 mm. to 2 cm. Of ten dogs nine recovered and were subjected to autopsy at periods from six to fourteen weeks after the operation. In all of these cases the stumps had increased in length and were dilated. They were all filled with bile. The wall showed some hypertrophy. In two of these cases the bile was inspissated and apparently beginning to form calculi.

They quote many other investigators who have also shown that dilatation occurs in such stumps. They also quote many human examples which have been previously reported in the literature, Kadian having collected twenty-eight such cases. They report two cases of their own.

A. J. W.

McEachern, J. D. Hepaticoduodenostomy for injury of the bile-ducts during cholecystectomy. *Ann. Surg.*, 1922, **75**, 344.

The author states that since the wider introduction of cholecystectomy there has been an increase in the number of injuries of the bile-passages. In only a small number of these cases is the injury recognized at operation, but it is generally shown later by a persistent fistula or evidence of obstruction of the duct. He points out that such accidents have often occurred in the hands of surgeons of wide repute. The possibility of this accident is greatly increased if there is a poor exposure in the operating field; sometimes it may be due to injury to the hepatic or the common bile-duct during attempts to clamp the cystic artery when it has been accidentally divided. The frequency of anatomical variations in this area also makes an accident much more possible. (It should be an invariable rule with the surgeon that no duct should ever be divided until the hepatic, cystic, and common ducts are all exposed and identified.) The author points out that whereas cholecystectomy is a relatively simple operation a reconstruction of the duct may be a most formidable procedure. The injuries fall into two main groups: those of obstruction of the duct and those of division. The type of operation employed will depend upon the extent and location of the injury. If sufficient duct be present the operation of choice is an end-to-end anastomosis over a rubber tube, for if the lower segment of the duct can be utilized the normal papillary entrance into the duodenum will prevent regurgitation and infection. If the ends cannot be brought into apposition Sullivan's operation of forming a new duct of omentum around a rubber tube may be tried, but it has the disadvantage that the new tube tends to become stenosed.

The difficulty lies in the identification of the distal end of the injured duct. In such circumstances an hepaticoduodenostomy should be performed.

The author quotes a case in which he carried out an operation of hepatico-duodenostomy where the hepatic duct was implanted directly into the duodenum much after the manner of Mayo, but an attempt was made to form a valve by suturing together anterior and posterior folds of the duodenum. Four days after the operation the patient became violent, and this was followed by the formation of a duodenal fistula which spontaneously closed three weeks later. Eight months after the operation the patient was in good health.
A. J. W.

FULLERTON, A. A modification of the operation of cholecystenterostomy. *Brit. M. J.*, 1922, i, 995.

Chronic pancreatitis which has led to an obstruction of the common bile-duct will necessitate the formation of a new passage for the flow of bile. The method which is usually used is that of cholecystenterostomy, but this operation has the drawbacks that: (1) The gall-bladder and its contents are infected and may remain so. This constitutes a grave danger to the health of the patient. (2) Gall-stones may form, or, if they have been removed, may recur. (3) The contents of the stomach, duodenum, or colon may regurgitate into the gall-bladder. To overcome these objections Fullerton advocates that the gall-bladder be opened and cleared of its contents. A light clamp is then placed near the neck of the bladder and the greater part of the viscus removed. The small remaining portion is anastomosed to the duodenum so that when the operation is completed the cystic duct opens into the duodenum without the intervention of any sac which might harbour gall-stones or regurgitated intestinal contents.

He reports a case where the above procedure was most satisfactory.
A. J. W.

WILLIS, A. MURAT. Relative merits of 'ideal cholecystotomy', cholecystectomy, and cholecystostomy. *Surg. Gynec. & Obst.*, 1922, **34**, 183.

In discussing the value of the above procedures the author considers gall-bladder cases in two broad groups. The first comprises those patients who are acutely ill, who are often elderly and frequently have some complication. His experience in such cases is in agreement with the general view to-day that a cholecystostomy is usually the operation of choice; for he states that, although this operation may not lead to a complete cure and may necessitate further operative steps, yet in such a patient the more severe and difficult operation of cholecystectomy is much more likely to be followed by a fatal result. In the second group are placed those patients who have only had mild symptoms, where the pathological changes are slight, and where there are no complications. It is in such cases that cholecystostomy would seem to be the operation of choice, but his experience has shown that this operation will often prove disappointing. He believes that this is in part due to the formation of adhesions after drainage, and he has therefore come to the conclusion that the operation of choice is a cholecystectomy. He considers, however, that normally the gall-bladder has very definite functions, so that if the inflammatory changes are slight it is doubtful whether cholecystectomy is justifiable. He therefore believes that there are certain cases, which must be carefully selected, where an 'ideal cholecystotomy' is indicated; the bladder being simply opened and explored and then closed without drainage. The suitable cases are those where the symptoms have been very few and where the gall-bladder appears to the eye to be normal. His experience shows that in such conditions the results of this operation are very satisfactory.

A. J. W.

Mathews, F. S., and **Others. Reconstruction of common bile-duct.** *Ann. Surg.*, 1922, **75**, 378.

At a meeting of the New York Surgical Society Mathews showed a patient who eight months previously had had her gall-bladder removed for some unknown condition, no stones being present. She had continued to drain bile externally since this operation. When seen by Mathews all bile was draining externally, and if the sinus closed for a short time there would be chills and fever. At the first operation the lower end of the hepatic duct alone was found and an attempt made to suture it to the under surface of the liver, which failed. Six months later a successful operation of reconstruction was carried out. The patient was then three months pregnant. The lower end of the duct was isolated, a tube inserted into its lateral aspect, and the other end inserted 3 inches into the liver and the end held in contact with the liver by means of chromic sutures. Bile ceased at once to escape from the wound. The patient made an uninterrupted recovery and the pregnancy continued.

At the same meeting Douglas reported a case of cholecystectomy with stones in the common duct. The opening in the duct was sutured, which was followed by drainage 6–7 weeks. About one year later the patient commenced to have jaundice, which steadily progressed, and at operation two years later the duct was found completely obliterated in one part. The two ends were opened and sutured together around a tube. The tube came away on the 12th day and the patient completely recovered.

J. F. Erdmann stated that he had had six similar cases, two of which died and four recovered. He sutured the duct around a small catheter.

S. Erdman reported another case in which the divided duct had been sutured around a T-tube. The patient remained well for six months, but later developed symptoms of stricture of the duct. A. J. W.

Judd, E. S. Bleeding ulcer of the duodenum associated with cholecystitis. *Ann. Surg.*, 1922, **75**, 459.

From time to time cases have been reported in the literature in which haemorrhage or melaena has occurred either in association with gall-stones or following operations upon an infected gall-bladder. In such cases an acute gastric or duodenal ulcer, due to the septic process, has usually developed. Cases have also been reported in which a chronic ulcer has shown an exacerbation with such a septic process and has given rise to severe bleeding. In the present communication Judd states that he has operated upon four cases with bleeding duodenal ulcer in which the pathological condition was more extensive in the gall-bladder than in the duodenum. In each case the duodenal ulcer could be demonstrated easily; in one case the amount of scar tissue showed that the ulcer was of long standing. The gall-bladders of all four patients showed cholecystitis and contained stones. The four cases were very similar, the chief symptom in each being gastro-intestinal haemorrhage, which was usually very severe.

None of the four had ever had severe pain. In one patient the haematemesis returned after a gastro-enterostomy done some years previously.

He reports at length another case where the patient had typical symptoms of gall-stones but had also had gastro-intestinal haemorrhage. Operation revealed chronic cholecystitis with stones and some oedema of the pyloric end of the stomach but no definite evidence of ulceration. Nevertheless, the haemorrhage ceased after cholecystectomy.

He states that Crispin, in the Mayo Clinic, found gastro-intestinal bleeding in about 5 per cent. of the cases of gall-bladder disease, and a later review of the cases occurring in 1918 and 1919 shows that haemorrhage was mentioned as a symptom in 2·43 per cent.

Rankin reviewed the histories of fifty-five patients in the same clinic who had gastro-intestinal bleeding, but in whom a pathological condition was found in the gall-bladder at operation. In the majority of males diagnoses had been made of gastric or duodenal ulcer. Thirty-seven of the patients gave a history of more or less typical gall-bladder disease, but in nine the history was very suggestive of an ulcer.

Judd believes that the bleeding is due to the effect of toxins from the infected gall-bladder or liver.

He gives a clinical history of the four cases. A. J. W.

Hall, A. J. **Splenomegaly with progressive ascites and loud venous hum.** *Brit. M. J.*, 1922, i, 592.

A remarkable case is reported of a young man of 25, who was a coal miner. His illness started with abdominal pain which after a few days was followed by a severe haematemesis of about three pints. He was kept in bed for six weeks, when he had another severe haematemesis. On examination he was found to have a very large spleen and profound secondary anaemia with the liability of gastro-intestinal haemorrhages. He developed ascites, and a loud venous hum was very evident over the lower part of the sternum. The anaemia continued and he had several attacks of epistaxis. The abdomen was tapped on several occasions with little relief. Except for the rapidity of the progress he seemed to be a typical case of Banti's disease.

After six months the abdomen had become greatly distended, and through the stretched areas the ascitic fluid began to ooze. This was followed by steady improvement. His pain disappeared and his appetite returned. He gained weight, and at the end of three months the oozing completely ceased and he was able to get about. Four years later he was in good health, well nourished, and able to work and enjoy life. The spleen, however, was still enlarged; there was no visible anaemia and no ascites. The venous hum was limited to an area the size of a halfpenny over the middle line opposite the sixth costal cartilage. A. J. W.

NEUROLOGY

Bassoe, P., and **Hassin, G. B.** **Myelitis and myelomalacia.** *Arch. Neurol. & Psych.*, 1921, **6**, 32.

Conclusions: Myelomalacia is not an inflammation but a degeneration of the spinal cord. The degenerative nerve-fibre changes are associated with progressive glia phenomena, principally of the nature of 'gitter' cell formation. The 'gitter' cells in this, as in any other type of secondary degeneration, are gliogenous in origin. Their task is to transform destroyed nerve-tissue into fat-like substances which they transport to mesodermic structures, such as blood-vessels and the pia. Reaching these structures, they are actively taken up by the proliferating adventitial and pial elements. From the adventitial and pial spaces they are carried to the subarachnoid space and thence to the blood for final elimination. The subarachnoid space is to be looked on as 'the dumping-ground' for any waste accumulated in the central nervous system. C. D. F.

Globus, J. H. **A contribution to the histopathology of porencephalus.** *Arch. Neurol. & Psych.*, 1921, **6**, 652.

Porencephaly is of interest partly because of the striking disproportion between the great loss of brain substance and the mild degree of functional disturbance, partly because of its close relationship with encephalitis. Globus's case was a well-developed male child of 11 months. His head was small and his extremities spastic in flexion with exaggerated deep reflexes. His parents had noted that he had not progressed mentally and that he seemed to be blind and deaf. The child died following an operation for bilateral subtemporal decompression, performed on the supposition of congenital microcephaly. At the autopsy it was found that the cerebral ventricles were markedly distended and that, with the exception of the frontal lobes, nothing was left of the cerebral hemispheres but a shell 2–3 mm. thick frontally and reduced to parchment-like thinness at the occipital pole. The basal ganglia were well developed; the corpus callosum present; the septum pellucidum thin, stretched, and fenestrated; the mid-brain, pons, medulla, and cerebellum of normal aspect. The soft meninges were in many places greatly thickened, in others oedematous and infiltrated with lymphocytes, macrophages, and a few plasma cells. Over the temporal region the pia-arachnoid was in process of fibrinous organization as shown by the presence of many fibroblasts and numerous mononuclear elements. Similar chronic and subacute lesions of inflammatory character with an added proliferation of neuroglia cells were found in the cortex of the frontal lobes as well as in the midbrain, pons, and medulla. Therefore the author comes to the conclusion that the porencephaly was due to an encephalitic process which, beginning in the latter part of intrauterine life, remained active and slowly progressive after childbirth. C. D. F.

Schaffer, K. Beiträge zur Lehre der zerebellaren Heredodegeneration. [**Contributions to the doctrine of cerebellar heredo-degeneration.**] *J. f. Psychol. u. Neurol.*, 1921, **27**, 12.

The collective term of heredo-degeneration has previously been used by the author (*Schweiz. Arch. f. Neurol. u. Psychiat.*, 1920, **7**, 193) to indicate various inter-related, hereditary, and degenerative disorders of the nervous system which are characterized by certain typical and common features such as the familial appearance, homochronicity, homotypism, and a more or less strikingly progressive course. These conditions were subdivided by R. Bing into: (1) types in which the degenerative manifestations are predominantly motor, including the spastic and dystrophic forms; (2) predominantly sensory, as in hereditary spinal and cerebellar ataxias; (3) predominantly psychic as in familial idiocy; (4) dyskinetic forms, including the myotonic, myoclonic, choreic, and tremor groups. The intrinsic nature of these hereditary forms is unknown. The histological findings, however, point to the existence of a close anatomical inter-relation similar to the close clinical relationship. In support of this suggestion Schaffer was able to emphasize the following points: (1) The process affects only the ectodermal components of the central nervous system. (2) It involves the cell processes and their corresponding bodies. (3) It is characterized by a marked swelling first of the cell bodies, then of the dendrons, and finally of the axons. Out of the twelve cases previously investigated only one showed alterations of the mesodermal constituents, and in this case the lesion was circumscribed and doubtless due to an inflammatory process of exogenous origin.

The two cases which are the subject of the present paper appear to support Schaffer's contention. The first was an idiot who was affected by an hereditary cerebellar ataxia without any trace of Friedreich's disease and who died of an intercurrent affection when 21 years of age. From an anatomical point of view the following malformations were noted: (*a*) Many deviations from the ordinary type of fissures and furrows of the brain convexity; (*b*) hypoplasia of the cerebral peduncles, cerebellum, and pons; (*c*) presence of binucleated nerve-cells in the cerebral cortex; (*d*) cytoarchitectonic alterations in the so-called association centres of Flechsig. The degenerative changes, which had evidently started in the cerebral hemispheres, had spread all along the cerebro-pontine-cerebellar system, while the motor and sensory regions of cerebral cortex and the systems of fibres connected with them appeared to be hardly affected. In the hypoplastic cerebellum degenerative changes were almost exclusively found in the hemispheres, viz. they had an essentially neo-cerebellar distribution. Histologically the degeneration was confined to the ectodermal components while the mesodermal elements did not appear altered in any way. This selective form of degeneration was particularly evident in the cerebral cortex, where it was characterized by a peculiar topographic distribution spreading from the external to the internal principal layers. As to the origin of such lesions two points are particularly emphasized by the author; first, the incomplete development of the cortex cerebri and cerebelli probably due to an original weakness of the neuroblasts which form the lamina corticalis (endogenous hereditary factor); second, a possible toxic influence acting on the nervous tissue during the early embryonic life as admitted by the school of v. Monakow (exogenous toxic factor). The second case was a woman of 41 years of age who died of an intercurrent affection after having exhibited for many years the picture of a typical cerebellar ataxia associated, in the end, with premature senility. She came from a family many members of which had been or were affected by the same malady. At the P.M. examination only a relatively moderate degree of atrophy of the cerebellar hemispheres was observed, while the histological investigation of the central nervous system revealed a double series of lesions consisting in a profound alteration of the nerve-cells of cerebral cortex, and in a complex systemic brain degeneration. The former, though extremely diffused, was particularly noticeable in the angular and fusiform convolutions and cornu ammonis, the layers from III to VI being most affected. The alteration itself was characterized by swelling of the cell bodies, wasting and disintegration of the Nissl granules whereby the spongioplasm was thrown into relief; and, at a farther stage, by transformation of these web-like structures into a fine granular detritus resulting finally in complete atrophy and destruction of the diseased nerve-cells. In the cerebellum the phylogenetically and ontogenetically younger portions in particular were affected by the degenerative process, the Purkinje and basket cells exhibiting the same pictures as observed in the cerebral cortex. The systemic lesion chiefly affected 'the intracentral cerebellar neurons, the sensory root protoneurons of pons and medulla oblongata as well as the pyramidal neurons'. In other words, the degeneration had a distinctly combined character, as one sees, for instance, in combined sclerosis of spinal cord involving the posterior and lateral columns. The difference consisted only in the fact that the heredo-degenerative process, instead of being primarily spinal, was in Schaffer's case primarily cerebral. In this case also, as in the former one, no lesions of the mesodermic elements were found, viz. the process was 'strictly parenchymatous, endogenous, and without trace of vascular reaction'.

C. D. F.

Bassoe, P., and **Hassin, G. B. Calcification of the cerebral vessels with a clinical picture simulating brain tumour.** *Arch. Neurol. & Psych.*, 1921, **6**, 359.

While calcification of large sclerotic vessels is extremely common as a general process, and calcification of a single vessel such as the renal, coronary, or femoral artery is not rare, there are few reports of a condition at all similar to that found in the present case. This is interesting in three respects: first, because a diagnosis of brain tumour was clinically justifiable and several operations were performed in the hope of removing the supposed tumour; second, because epileptiform fits were the principal symptoms, and the case indicates what kind of changes may occasionally cause such attacks; third and chiefly, because the pathological lesion was most unusual, and consisted essentially in the presence of a large indurated area in the interior of the left hemisphere. Changes were particularly pronounced in the mesodermic tissues such as capillaries, larger blood-vessels, and pia-arachnoid, and somewhat less marked in the parenchyma, where numerous foci of secondary nerve-degeneration and accumulations of large masses of lipoid substances were observed. Both parenchymatous and mesodermal changes were associated with old haemorrhagic foci and vast deposits of lime salts. The haemorrhages were accidental, the result of three operations. The calcifications were more or less confined to the capillaries, the larger blood-vessels showing only here and there the presence of calcareous masses, which were limited to the adventitial spaces. The precise condition of the pia-arachnoid could not be ascertained in consequence of the traumatic haemorrhages. According to the authors, the condition of both capillaries and larger blood-vessels was altogether unique and different from that observed in syphilis, endarteritis obliterans, so-called calcium metastases, arteriosclerosis, and purely inflammatory states. The authors particularly emphasize the fact that the calcareous deposits occupied areas infiltrated with a colloidal or hyaline substance considered by them as a result of primary degeneration which had preceded and rendered possible the subsequent deposit of calcareous matter.

C. D. F.

Uyematsu, S. A study of the cortical olfactory centre. *Arch. Neurol. & Psych.*, 1921, **6**, 126.

In spite of the efforts of many authors, the exact location of the cortical olfactory centre cannot be said to have been definitely determined. Recently the author had the opportunity of investigating two cases of unilateral involvement of the olfactory lobe, one of congenital absence, the other of softening due to arteriosclerosis. In both cases a well-marked degeneration of the anterior part of the lobus pyriformis was found. Evidence is adduced by the author showing that the lesion could be reasonably regarded as secondary to the primary involvement of the peripheral olfactory centre. He therefore comes to the conclusion that the lobus pyriformis must be the chief olfactory centre in the human brain. The cornu ammonis and the rest of the limbic lobe showed little evidence of degeneration, and the author has nothing to offer from the present study as to the functional importance of these parts. C. D. F.

Buscaino, V. M. (1). I dati attuali sull'anatomia patologica del sistema nervoso dei dementi precoci. [**On the histopathology of the nervous system in dementia praecox.**] *Riv. di patol. nerv.*, 1921, **26**, 87.

Buscaino, V. M. (2). Nuovi dati sulla distribuzione e sulla genesi delle zolle di disintegrazione a grappolo dei dementi precoci. [**Fresh observations on the distribution and origin of aciniform areas of disintegration in dementia praecox.**] *Ibid.*, 1921, **26**, 57.

Buscaino, V. M. (3). Le cause anatomo-patologiche delle manifestazioni schizofreniche nella demenza precoce. [**Pathological cause of schizophrenic manifestations in dementia praecox.**] *Ibid.*, 1920–21, **25**, 197.

The first of Buscaino's papers is a review of our present state of knowledge of the morbid anatomy and histopathology of the nervous system in dementia praecox. It is important because of the rich bibliography which it contains and because of the critical discussion of the results obtained by different authors in 550 autopsies. Buscaino's conclusions are: in most cases of dementia praecox an abnormal constitution of the nervous system is anatomically demonstrable. The supposition that the malady may be due to inflammatory changes either of the meninges, of the blood-vessels, or of the nerve-substance is untenable. The various lesions as described by different authors can be considered as degenerative in character. In the cerebral cortex the most affected layers are the sixth, fifth, and third; but their alteration does not satisfactorily explain the disorders of the association process so characteristic of the disease. In many cases, lesions of the corpus striatum have been observed which may account for the muscular hypertonus of the catatonic forms. The very frequent troubles in the 'vegetative' sphere are probably connected with degenerative changes of the grey matter of the medulla oblongata, spinal cord, and sympathetic ganglia, to which no sufficient attention has, as yet, been paid.

The other two papers of Buscaino are chiefly concerned with the description of a peculiar lesion of the white substance of cerebral cortex, basal ganglia, midbrain, cerebellum and pons, for which the term 'aciniform areas of disintegration' is proposed. These are found among nerve-fibres, most frequently next to blood-vessels, and appear to consist of a more or less amorphous material contained within a meshwork of neuroglia fibres. Sometimes nuclei of neuroglia cells and fragments of nerve-fibres and occasionally of nerve-cells are seen either within or at the edges of the disintegration zones. For their demonstration formalin material or pieces fixed by means of 5 per cent. nitric acid in absolute alcohol can be used. After embedding in paraffin, sections are stained either for 18 hours with a 1:2,000 solution of toluidin blue, or for three minutes with Ziveri's fluid (saturated solution of picric acid 100 gm. with 0·05 gm. of methylene blue and 0·10 gm. of acid fuchsin). By the first method the substance of the disintegration areas is stained violet-red, by the second bright yellow. Control specimens prepared by Spielmeyer's method for medullated fibres show, in places corresponding to the disintegration areas, zones of demyelinization the central portion of which is occupied by an amorphous detritus. The disintegration areas vary in number and particularly in size, some of them being recognizable only with the help of the microscope, others reaching such dimensions as to be visible to the naked eye. The author was not able to ascertain the nature of the amorphous material to which the areas are essentially due. However, he points out that it is not dissolved by nitric acid, alcohol, or xylol, and that it does not stain with acid fuchsin, methylene blue, or eosin; it does not contain iron and does not take the silver by Bielschowsky's method. It is morphologically different from Reich's π granules and microchemically from Bonfilio's basophilo-metachromatic substance α. It has a certain similarity to the giant masses of basophilo-metachromatic substance observed by Baroncini in a case of atypical psychosis. (For references and details as to these various degenerative products see Alzheimer, *Histol. u. histopath. Arb. über d. Grosshirnr.*, 1910, iii, 401). Generally the 'aciniform areas of disintegration' appear to be due to a primary form of degeneration of nerve-fibres, which affects first the axis cylinders and then the medullary sheaths. As shown by various sets of experiments made by the author for the purpose, the disintegration areas are neither artefacts due to fixing or other reagents nor agonal or cadaveric alterations; but can be re-obtained in dogs by poisoning with formic acid. The author attributes to the described areas a considerable importance, as they might explain, better than any other lesion, the profound disorders of the association process. However, he himself points out that similar areas were observed by him, though in a much smaller number, in cases of acute delirium and G. P. I. It may be added that they much remind one of the spotty atrophy of medullated nerve-fibres described by Borda, Fisher, and Bielschowsky in cases of G. P. I. and senile dementia. C. D. F.

BACTERIOLOGY

Lumière, A. Choc antianaphylactique et colloidoclasie. [**Anti-anaphylaxis and colloidoclasis.**] *Presse méd.*, 1921, **29**, 960–1.

Lumière has for some time held that colloidoclasis is to be explained on a physical basis, namely, by the stimulation of the cerebral vascular endothelium by flocculent precipitates formed by the interaction of the antigen and the serum of sensitized persons. In his view this stimulation is followed by dilatation of the cerebral vessels and by a reflex dilatation of vessels in other parts of the body. From this follows a profound fall of blood-pressure and all its consequence.

Widal has raised objections to this theory and in this paper Lumière answers them. Widal's first objection is that no one has ever succeeded in seeing these flocculations. Lumière replies that they are of the same density as the serum in which they are suspended and so have escaped notice, but claims that he can now demonstrate them by the ultra-microscope.

Secondly, Widal objects that this purely physical theory does not explain the action of minute desensitizing doses. Lumière replies that in fact his theory amply accounts for this, on the supposition that the desensitizing dose accustoms the nerve-tissue to the presence of flocculations and so prevents an explosive reaction. He cites the fact that one can bear the foot in water brought slowly to a heat of 45–46° C., whereas if the other foot, which has not been slowly habituated, be suddenly plunged in the water great pain is felt.

Finally, Lumière carries the war into the enemy's country and attacks the theory of Widal that colloidoclasis depends on rupture of the equilibrium of the colloids of the endothelial cells. To disprove this he shows that he can produce a solution of inert barium sulphate which is innocuous so long as the particles are evenly divided, but produces shock if any flocculation is present, as is normally the case in a solution or suspension not specially prepared. Barium sulphate, oils, albumins, and various other substances which produce shock have, he says, no single feature in common except flocculation. He concludes that all the measures which experience shows to be efficacious in preventing or remedying shock have their efficacy explained on his theory alone. G. W.

Jülich, W. Zur Differentialdiagnose hochfieberhafter, mit Leukopenie einhergehender Erkrankungen. [**The differential diagnosis in hyperpyrexia with leucopenia early in a disease.**] *Beitr. z. Klin. d. Tuberk.*, 1922, **50**, 303–10.

Jülich has carried out blood counts in 14 cases of hyperpyrexia in which the diagnosis at the onset of the disease was obscure. The tuberculous nature of the disease transpired later. In every case the contrast between the high fever and the low leucocyte count was marked. Jülich finds that the leucocyte count is of great value in prognosis and that it is bad when, in the course of the disease, there is a progressive (relative) 'polynucleosis' associated with lymphopenia, diminution of the number of mononuclear cells, and diminution or absence of the eosinophils. On the other hand, a good prognosis is indicated by a relative lymphocytosis and diminution of the polynuclear cells, and by an increase in the number of the eosinophil cells. C. L.

Müller, O., u. **Brösamlen, O.** Die Bluteosinophilie als Indikator für jeweilige Reaktionsfähigkeit des Organismus. [**Eosinophilia as an index to the organism's reaction capacity from time to time.**] *Beitr. z. Klin. d. Tuberk.*, 1922, **50**, 289–302.

Müller and Brösamlen refer to the difficulty of selecting cases suitable for tuberculin treatment and to the need for objective criteria both for the selection of cases and the control of treatment. Eosinophil counts made in a great number of cases undergoing various forms of vaccine treatment have convinced them that the eosinophil leucocyte is a very reliable guide. The eosinophil leucocyte also shows whether vaccine treatment should be cautious or drastic, and when it should be discontinued. When the eosinophil curve shows a rapid and definite rise during any kind of treatment, this may be carefully pushed farther. But if it has no definite effect on this curve, the treatment that is being given should not be pushed any farther, and if the curve shows a downward tendency, the treatment should be discontinued at once. C. L.

Filinski, W. L'augmentation du taux de la globuline dans le sérum du sang comme résultat de l'insuffisance hépatique. [**Increase of the titre of globulin in the blood-serum, resulting from hepatic insufficiency.**] *Presse méd.*, 1922, **30**, 236–7.

Filinski concludes as follows from a study of the proportions of the albuminous constituents of the blood-serum: (*a*) there is no regular disturbance of their relative proportions in cachexia or cancer, and (*b*) no diagnosis of cancer can be based on such disturbances, which (*c*) are probably due to an increase of globulin dependent on hepatic insufficiency. G. W.

Cramer, W., Drew, A. H., and **Mottram, J. C.** **On the function of lymphoid tissue in nutrition.** *Lancet*, 1921, ii, 1202–8.

Cramer and his collaborators conclude that absence of the water-soluble vitamin B from the diet leads to an atrophy of the lymphoid tissue throughout the body. It is upon this resulting deficiency of lymphoid tissue that clinical signs of deficiency disease depend. They consider that this vitamin is necessary for the maintenance of life in a highly differentiated animal, not because it is required for every cell but because without it the lymphoid tissue fails. Further, the lesions of lymphoid tissue which may be produced by absence of the water-soluble B vitamin may equally be produced by other factors and are not to be regarded as specific. G. W.

Roch, M., et **Gauthier, P.** Choc hémoclasique chez les pleurétiques et les ascitiques par auto-injection du liquide de l'épanchement. [**Hemoclasic shock by the auto-injection of the exudates in cases of pleurisy and ascites.**] *Presse méd.*, 1922, **30**, 209–10.

The treatment of pleurisy and ascites by injections beneath the skin of a few c.cm. of the fluid removed has been practised for some years. The results have always been uncertain, sometimes dramatically successful and at others entirely negative. Roch and Gauthier have examined this treatment afresh in the light of recently gained knowledge of haemoclasis and protein therapy. In ten cases they found by estimation of the blood-pressure and leucocyte count that there was distinct evidence of haemoclasis. G. W.

Oftedal, S. Multiple myeloma. *J. Am. M. Ass.*, 1921, **77**, 1547.

Oftedal adds one more to the reported cases of multiple myeloma. Bence-Jones proteinuria was present. ‘General Roentgen-ray examination’ disclosed these rarefied areas in several of the bones of the upper part of the body, particularly the clavicles, sternum, ribs, left humerus, and skull. A fracture of the left humerus healed readily but soon broke down again. Before the patient’s death some of these tumours had grown to a large size and the sternum was so soft that it could be pitted by finger pressure. The histological examination of these tumours showed that they were very highly cellular and the cells seem to have been of the plasma-cell type.

G. W.

Thiel, G. A., and Downey, H. The development of the mammalian spleen. [**B.**] *Am. J. Anat.*, 1921, **28**, 279–333.

The authors state that the spleen first appears as a dense mass of tissue in the mesentery and its earliest vessels are branches of the splenic artery. In 3–4 cm. pig embryos, before the open adult circulation is fully established, the blood-forming activity of the spleen commences. Cells of the mesenchyme which bear no definite relation to vessels or sinuses become more basophilic and lose their connexion with the mesenchymal syncytium. These cells become the ‘large lymphocytes’ which are typical of the early stages of all haemopoietic organs. Erythropoietic activity is first recognized in the presence of erythroblasts in the lacunae left by the separation of large lymphocytes from the primitive syncytial mass. These are at some distance from the sinuses, but at a later stage a few erythroblasts may be formed from the margins of sinuses. Granulocytes are rare in the pig’s spleen at any time. Lymphocyte formation is exemplified in the formation of a lymphoid sheath around arteries. At first this sheath is a dense tissue, but later resolves into a loose network, the meshes of which are packed with small lymphocytes. These are differentiated directly from the mesenchyme and do not pass through a ‘large lymphocyte’ stage. There are thus two haemopoietic systems in the fully developed spleen, but both originate in the same mesenchyme and the free cells of the lymphoid system migrate into the pulp. G. W.

Elving, H. Om medel att öka blodets koagulationsförmåga. [B.] [**Concerning devices for increasing the coagulability of the blood.**] *Finska Läk-sällsk. Handl.*, 1921, **63**, 551.

At the Surgical Department of the Communal Maria Sjukhus in Helsingfors, Elving has tested the action of various haemostatics. He employed Bürker’s method, and he first investigated the variations in the rate of coagulation of the blood in healthy persons at different hours of the day. The slight increase (5·1 per cent.) observed in the rate of coagulation at midday could probably be explained as being within the range of errors of technique. Only in 1 out of 12 cases did X-ray treatment of the spleen fail to effect a considerable increase in the coagulability of the blood. This increase was greatest about four hours after an exposure, and it was still considerable after 8 hours; a gradual decrease was observed from this stage onwards, but in several cases even after 24 hours of an exposure the rate of coagulation was still slightly above normal. The greatest increase effected by the X-rays was 67 per cent., and the usual increase ranged between 25 and 40 per cent. A similar, but less marked, effect was obtained by X-ray treatment of the liver and heart. The cases thus treated showed a diminution in the number of lymphocytes. It was found that the prophylactic treatment of patients with the X-rays 4 to 5 hours before operation was in some cases remarkably effective in preventing loss of blood.

With regard to other devices for increasing the rate of coagulation of blood, Elving found that large doses of sodium chloride (20 c.cm. of a 10 per cent. solution) considerably increase the rate of coagulation (up to 27·3 per cent.), whereas the action of small doses is uncertain. But calcium chloride seems to be far superior to sodium chloride as a haemostatic, and the intravenous injection of 20 c.cm. of a 15 per cent. solution, i. e. 3 gm. of calcium chloride, almost doubles the rate of coagulation. In one case the intravenous injection of 10 c.cm. of a 10 per cent. solution increased the rate of coagulation by 91 per cent. Elving has adopted this procedure with marked success in cases of haemorrhage from the lungs, stomach, intestines, and kidneys, and has also found it useful as a prophylactic an hour or two before operations at which much loss of blood is anticipated. Another series of investigations concerned the diuretic euphyllin, recommended by Nonnenbruch and Szyzka as a haemostatic. This it certainly is, an intravenous injection of 0·5 to 0·75 gm. increasing the rate of coagulation up to 88·9 per cent. But the severe tachycardia simultaneously provoked rendered the therapeutic exploitation of this drug as a haemostatic of dubious value. Elving concludes that increasing the rate of coagulation by the X-rays is still in the experimental stage, and the time has not yet come for its general clinical adoption. A drawback to the intravenous injection of sodium chloride is the fact that it acts as a haemostatic only in large doses; the best haemostatic known at present is calcium chloride injected into a vein in the dosage already indicated. C. L.

Ringoen, A. R. The origin of the eosinophil leucocytes of mammals. *Fol. Hemat.*, 1921, **27**, 10–68.

Ringoen contributes a long and valuable paper on the origin of eosinophil leucocytes and their relationship to mast cells. He concludes that each of these is a distinct and independent cell, following its own line of development. He obtained no evidence that eosinophil granules could be derived from haemoglobin, but, on the contrary, much evidence pointing in the opposite direction. He considers that eosinophilia following injections of egg white, &c., is to be regarded as a response to anaphylaxis. G. W.

Hill, A. V. The 'buffering' of blood. *Brit. M. J.*, 1922, i, 340–1.

The reaction, i. e. the hydrogen-ion concentration, of the blood is comparatively little altered by the addition of quantities of acid which would seriously alter solutions of a neutral salt. This is due to 'buffer' substances in the blood, and Hill discusses the nature of these. They reside more especially in the red cells, and consist in very weak basic salts of carbonic and phosphoric acid. On the addition of further acid these salts part with a portion of their base, e. g. alkaline phosphate becomes acid phosphate, and the base freed is available for combination with the added acid. The total result on the reaction of the blood where such weak acids are in question is almost nil, so that the added acid is dealt with with little change in hydrogen-ion concentration. It is obvious that if the buffers were completely effectual the addition of acid would have no effect, if they were entirely absent the reaction would change in proportion to the acid added. In the human body the buffer salts and the action of the kidneys (excreting surplus products) maintain a constant curve between these extremes, a curve of which the height but not the form (the 'curve' is in fact a straight line) is altered by the amount of acid phosphate, acid haemoglobin, &c., available. This in turn depends to a large extent upon the number of red cells present. A study of the variations in this buffer curve should be productive of most interesting results. G. W.

Sacchetto, I. Le alterazioni del fegato da lesioni spleniche studiate colla colorazione vitale. [**Use of intra-vitam staining methods for the study of liver changes due to splenic lesions.**] *Gazz. d. osp.*, 1921, **42**, 281.

Experiments were made in rabbits in the spleen of which focal lesions were caused by freezing with ethyl-chloride. After the shock of the operation was over, one or two injections of a variable quantity of a half-saturated solution of lithium carmine were made intravenously into the same animals, which were killed 12 hours afterwards. The histological examination of the liver showed that altered cells and necrotic products had passed, through the splenic and portal veins, from the spleen into the liver, where they had caused regressive changes of the liver-cells. The changes were limited to small areas which, during a second period, became the site of small-celled infiltrations and of active proliferations of the connective tissue. Areas such as those described appeared and evolved at irregular intervals and in changing numbers in different animals. The lesions had, on the whole, a striking similarity with those of Laennec's cirrhosis.

C. D. F.

Katz, G. Die Senkung der roten Blutkörperchen im Zitratblut bei Lungentuberkulose. [**The sedimentation of red blood-cells in citrated blood in pulmonary tuberculosis.**] *Ztschr. f. Tuberk.*, 1922, **35**, 401–24.

Katz has investigated the rate of sedimentation (S.R.) of the red cells in 109 persons, repeating the test as often as 8 times in several cases. In 64 cases both the S.R. and the clinical examination indicated pulmonary tuberculosis; in 23 cases the S.R. was an aid to the clinical examination in excluding active pulmonary tuberculosis. Katz agrees with earlier writers in regarding the fibrinogen content of the blood as the most important factor in the S.R., and the fibrinogen content being directly proportional to the degree of tissue destruction in the body, the S.R. becomes an accurate guide to pathological metabolism. Extensive burns, malignant tumours, pneumonia, active syphilis, and every other morbid condition promoting tissue destruction are reflected in the S.R., which is no more specific for active pulmonary tuberculosis than a high temperature, pulse- and respiration-rate. Following Westergren's technique (*Acta Med. Scand.*, 1921, **54**, 247), Katz finds sedimentation normally takes 8 to 9 hours, the extremes being 40 to 50 minutes and 24 hours. Katz publishes charts showing the parallelism of the S.R. and the temperature from time to time. As the S.R. curve continues to fall a considerable time after the temperature has returned to normal, the former is a more reliable guide to treatment. In other words, pathological destruction of tissues may proceed for some time after the temperature has reached normal, and many a complication and relapse may be avoided if the S.R. instead of the temperature is taken as a guide to the treatment of such acute diseases as diphtheria, influenza, broncho-pneumonia, &c. In one case of sore throat and in another of influenza with broncho-pneumonic foci, the patients insisted on their discharge, all the clinical manifestations showing improvement. But the S.R. was still above normal, and 10 days later both cases relapsed. As the rate of sedimentation varies within such wide limits as 2 to 130 mm. per hour, the test is extraordinarily delicate, and in an acute disease like pneumonia the changes in the S.R. are very great from day to day. Among cases of emphysema and chronic bronchitis systematically examined by the S.R., there were two which were suspected of being associated with chronic phthisis because the S.R. was abnormally high; this suspicion was subsequently confirmed by clinical and X-ray examination. Provided other pathological conditions can be excluded in cases of tuberculosis, a high S.R. is invariably indicative of activity of tuberculosis. Conversely, a normal S.R. shows that tuberculosis is either latent or non-existent. When, in cases of pneumonia and pleurisy, a high S.R. falls to normal, there is no tuberculosis, or it has again become latent. Thus, though the S.R. is not specific, it is a delicate test of considerable practical value in tuberculosis.

C. L.

Lecomte du Noüy, P. Spontaneous decrease of the surface tension of serum. *J. Exper. M.*, 1922, **35**, 575.

When a serum is exposed to the air, the surface tension of its free surface decreases progressively according to a certain law, until after about ten minutes a state of equilibrium is attained. The purport of this paper is to report a study of this phenomenon. The existence of a film at the surface of protein solutions has been discussed by Ramsden, who, according to the above author, neither observed nor measured any lowering in the surface tension of the serum, nor noticed the variations of the surface tension of water plus serum as a function of the time.

Over 3,000 measurements were made by the author, using his 'tensiometer', described in the *J. Gen. Physiol.*, 1918–19, **1**, 521. The apparatus is based on the adhesion of a platinum ring to the surface of the liquid and the stress necessary to tear off the film is measured by the tension of a steel wire. If γ is the value of the surface tension in dynes per cm. and t is the time, then the experimental curves show that $d\gamma/dt$ progressively decreases.

Generally, after about ten minutes the surface tension reached a practically constant value. After stirring, a rise occurs and a similar phenomenon takes place. Stability is, however, not so rapidly attained, requiring about 25 minutes. By stirring again the same thing happens repeatedly, the slope of the curve being less marked each time, the rise in surface tension being slightly below each previous value. The phenomenon seems to undergo a sort of damping. Prolonged heat, at 55° C., and time seem to inhibit the phenomenon. When precipitation occurs in a serum, the bottom of the liquid, which contains the precipitate, has the highest surface tension. If stirred, the surface tension rises a little every time. The clear upper part, with lower surface tension, shows the reverse phenomenon: after every stirring, the surface tension becomes a little lower.

The hypothesis of surface coagulation, or the formation of a homogeneous solid film, does not, according to the author, account for any of the phenomena studied. It is possible that temperature and evaporation play a part, but it is shown that their effect is negligible.

Then follows a discussion of Willard Gibbs's adsorption formula $u = -\frac{c}{RT} \cdot \frac{d\gamma}{dc}$ where u is the quantity adsorbed, c the concentration, R is the gas constant, T the absolute temperature, and γ the surface tension. An attempt was made to establish a general equation on a purely empirical basis, which would express the phenomenon in all cases, before and after stirring, with only one coefficient. Such a one was found in $\gamma = \gamma_0 \epsilon^{-Kt^{\frac{1}{2}}}$ where K is the constant. The experimental and calculated values agree to within 0·2 per cent. If the factor t is changed to c (the concentration) it satisfactorily expresses, in general, the phenomena of adsorption in the surface layer. W. A. M. S.

Cremona, P. Sul valore della siero-bleu-metilene reazione. [**On the value of sero-methylene blue reaction.**] *Pathologica*, 1922, **14**, 44.

The sero-methylene blue reaction investigated by the author is a modification of that proposed by Russo for urine (*Riforma med.*, 1905, **21**, 507). A 1 : 1,000 filtered solution of methylene blue in distilled water is the only reagent necessary for carrying it out. Four drops of this solution are added to 4 or 5 c.cm. of serum contained in a test-tube to be shaken after the addition of each drop of reagent. The serum may assume different shades of colour from deep blue to bright or emerald green. When the colour is decidedly green the reaction is said to be positive. Working with this method, the author (who apparently was looking for a very simple glanders test) obtained the following results: In normal animals (horses, cows, oxen, pigs, &c.), either when working or resting or in various physiological conditions, the sero-methylene blue reaction is constantly negative whether the serum is previously warmed at 56° C. or not. Maximal doses of pilocarpine, caffeine, quinine, eserine, do not affect the reaction which, in the case of normal animals, remains negative also after the injection of mallein and tuberculin. In horses affected by glanders the reaction is constantly positive, and becomes negative about 4 to 8 hours after an injection of mallein. In other infectious diseases and toxic states the reaction is sometimes positive, sometimes negative. The reaction is, therefore, not specific of glanders, but has a considerable practical value increased by its extreme simplicity of execution. C. D. F.

Leinati, L. La fagocitosi leucocitaria negli animali castrati. [**On phagocytosis after castration.**] *Pathologica*, 1922, **14**, 22.

Experiments were made in normal and emasculated dogs. Leucocytes were obtained in various ways from the animals experimented upon, and then mixed with a double quantity of a killed emulsion of *S. pyogenes albus*, and the mixture kept for half an hour at 37° C. Stained preparations were then made and all the germs contained within 100 leucocytes counted each time. If the total number of germs counted in each experiment is termed N^1 and the number of leucocytes considered is called N, the result of $\frac{N^1}{N}$

will be a variable quantity, termed by the author phagocytic index (indicated as *I. F.* from the Italian *indice fagocitario*). The interesting conclusions reached are: both unilateral and bilateral castration cause a constant diminution of the phagocytic index. But when the operation is performed on one side only the diminution is not so remarkable and in course of time the phagocytic index reacquires normal values, while the effect of the removal of both testes is apparently permanent. If after bilateral castration an homologous testis extract is injected intraperitoneally, the phagocytic index shows an increase, which lasts, however, only 24 hours, when it returns to its previous low value. According to the author, these facts appear intimately connected with a biological decay of leucocytes in consequence of castration. C. D. F.

Pellegrini, R. Importanza dei movimenti attivi delle pareti vasali per la migrazione del sangue nel cadavere e per la formazione delle ipostasi. [**Importance of active movements of blood-vessel walls for the migration of blood in the dead body and the production of post-mortem hypostatic congestion.**] *Pathologica*, 1922, **14**, 16.

Experimental investigations in rabbits. After death has taken place the wall of blood-vessels continues to contract spontaneously, sometimes for some hours. The hypostatic congestion of the dead body is therefore due not only to gravitation and supervening cadaveric rigidity of striated muscles and muscular coats of arteries, but also to post-mortem active movements of the wall of blood-vessels. C. D. F.

Campora, G. Sopra un caso di neoformazione fibrosa dell' encefalo a tipo cheloideo per ferita d' arma da fuoco. [**Fibrous growth of the cheloid type in the brain from a case of wound from a firearm.**] *Riv. d. patol. nerv.*, 1921, **26**, 79.

The new growth had the aspect of a tumour and had reached the size of a walnut. It was continuous with the cicatricial tissue consequent upon a cerebral wound from a firearm. This had been inflicted eight years before the accidental death of the patient, who was only 15 years of age when wounded. The development of the cheloid is by the author put tentatively in connexion with this last fact. The case is interesting because of the extreme rarity of observations of the sort and of the indirect light it throws on the aetiology of benign tumours of the brain substances. C. D. F.

Busacca, A. Sulla pretesa riviviscenza del connettivo negli innesti di pezzi fissati. II. [**On the supposed revivification of the connective tissue in grafts of fixed pieces. II.**] *Arch. per le sc. med.*, 1921, **44**, 157.

Polettini, B. Sulle modificazioni di colorabilità dei tessuti fissati conservati in diversi liquidi. [**On changes in the staining power of fixed tissues kept in different fluids.**] *Pathologica*, 1921, **13**, 392.

Busacca's paper is a continuation of previous work for which see *Giorn. d. r. Accad. di med. di Torino*, 1920, **83**, 96, and *Arch. per le sc. med.*, 1920, **43**, 128. In his earlier contributions the author had set forth the actual state of the question from a histological point of view and with particular reference to the important works of Nageotte. He gave, in addition, an account of some personal experiments on the destiny of fragments of nerves fixed in alcohol and grafted between the stumps of cut nerves either of rabbits or of dogs. As a result of these experiments the author came to the conclusion that the dead grafts may remain unaltered for long periods between the stumps of cut nerves, but that in course of time they undergo regressive changes and are finally reabsorbed through the medium of phagocytes. These manifest their action particularly on the axis cylinders and myelin of the fixed grafts, while the connective tissue laminae behave like inert bodies which oppose a great resistance to destruction though not causing any noticeable inflammatory reaction. They appear on the contrary to have a favourable 'stereotropic' action on the axis cylinders growing from the living central stump of the host and proceeding along the laminae of the perineurium and septa of the endoneurium of the fixed grafts, particularly where phagocytes have prepared the way. The influence of the grafts was, therefore, found to be beneficial also in saving the regenerating fibres from the deviations due to cicatricial tissue forming between the two stumps after simple sections of a nerve. If, instead of pieces of nerves, fragments of fixed tendons are grafted between the stumps of a cut nerve the dead tendon fibres oppose a very great resistance to the progress of the newly-formed axis cylinders, which are thus compelled to deviate in various ways in order to reach the peripheral stump and reconstruct the interrupted nerve-path. In addition, it is not quite clear what is the final destiny of the grafted and apparently inert fragments of tendon persisting unaltered for extremely long periods within the living tissues of the host. A similar process takes place when pieces of tendons fixed in alcohol are grafted between the stumps of a cut tendon. If the grafts are soft enough, as happens in the case of young rabbits' tendons, they are invaded at first by fibroblasts and then by newly-formed tendon fibres which originate from the host and rebuild the interrupted path, while the grafts are reabsorbed. If the grafts are very compact and hard, as in the case of dogs' tendons, fibroblasts are unable to penetrate into them, but newly-formed tendon fibres equally proceed along them and apparently become so intimately connected with those of the grafts that after a time a histological distinction between fixed and living fibres is extremely difficult if not impossible. On the whole, these various experiments entirely confirm the results obtained by Nageotte and the great importance that grafts of fixed tissues have from a surgical point of view. Only Nageotte's theory of the revivification of dead and fixed connective tissues appears untenable.

Polettini's experiments consisted of the grafting of fixed pieces of tendons, cornea, cartilage, and arteries (see *Pathologica*, 1920, **12**, 415). His results and conclusions were similar to those of Busacca, particularly as regards the beneficial influence of dead grafts on the restoration of function, e.g. of cut tendons. In addition, he had observed, like Nageotte, that fragments of fixed tissues, once grafted among living ones, lost, little by little, their staining power. In order to study more closely this phenomenon he endeavoured to make various experiments *in vitro*, an account of which he gives in the present paper. Pieces of cornea, aorta, auricular cartilage, and bone from dogs, rabbits, and guinea-pigs were fixed in 10 per cent. formalin and kept for a certain time in 95 per cent. alcohol. They were then washed with sterile physiological salt solution and distributed among many test-tubes containing either physiological salt solution, or blood-serum, or fluid culture media, some of which were, in addition, inoculated with *B. coli communis*, *S. pyogenes aureus*, and an imperfectly identified anaerobic bacillus. The tubes were kept at different temperatures and the pieces histologically examined after various periods of time. It was found that fixed tissues may lose their staining property *in vitro* as *in vivo*. A temperature of 37° C. is necessary for the production of the phenomenon which manifests itself after about 20 days if the tissues are kept in homologous or heterologous sterile serum, and after about 9 days if serum cultures or broth cultures are used for the experiment. The same fact occurs when tissues are kept in serum inactivated at 56° C. and in serum mixed with chloroform. But it cannot be observed in pieces left from 100 to 150 days either in the same fluids kept at about 5° C., or in sterile citrated blood, Tarozzi's sterile bouillon, and sterile physiological solution, even when maintained all the time at 37° C. From these results Polettini concludes that the loss of the staining power in grafts of fixed tissues is probably due to conditions and substances connected with the metabolism of the living elements of the host. Of these conditions and substances only the temperature factor could be, for the time being, ascertained.

C. D. F.

Luna, G. Studio sulle cellule pigmentate della coroide coltivate *in vitro*. **[Cultures *in vitro* of the pigmented cells of the choroid.]** *Arch. Ital. anat. e embry.*, 1921, **18**, 146.

The pigmented cells of the choroid may be cultivated *in vitro* in homologous blood-plasma. About two or three hours after the culture is made the young cells begin to migrate from the implantation point. The migration continues in the following periods though in a rather sluggish manner, which is probably due to the great number of pigment granules they contain. As they migrate they do not change form as in the case of other mesenchymal cells, but have a distinct tendency to maintain their original shape. The pigmented cells of the choroid sometimes fuse with other mesenchymal cells present in the same cultures. This shows that a certain degree of attraction may exist among elements of relatively different nature. In old cultures the pigment granules appear variously modified. In some cases they are transformed into refracting droplets which stain with iron haematoxylin but not with Sudan III; in other cases they lose their original colour and size and appear as much smaller granules. These stain blue with iron haematoxylin and red by Altmann-Kull's method. For this reason the author thinks that the minute granules are mitochondria and that they represent a sort of stroma on which pigment had been deposited during development. This agrees with the results obtained by other authors by the study of the normal evolution of the pigmented cells of the choroid in chick embryos, and gives a hint as to the significance of the refracting droplets above mentioned. These may be swollen and altered mitochondria, a supposition in agreement with the facts observed by Murray in a transplantable liposarcoma of the guinea-pig (*J. Path. & Bact.*, 1906, **20**, 260), Romeis in the spermatozoa of *Ascaris megalocephala* (*Arch. mikr. Anat.*, 1912, **80**, Abt. II, 129), and D'Agata in various tissues in pathological conditions (*Intern. Monatschr. Anat.*, 1913, **29**, 443).

C. D. F.

Salvioli, I., e **Sacchetto, I.** Ricerche sul metabolismo dei lipoidi e dei grassi nelle cellule epatiche di animali digiunanti od avvelenati con fosforo. [**Investigations on metabolism of lipoids and fats in the liver-cells of animals either fasting or poisoned with phosphorus.**] *Gazz. d. osp.*, 1921, **42**, 828.

Neutral fats and fatty acids, which are normally present in the liver-cells of dogs and guinea-pigs, progressively disappear when such animals are kept fasting. Their place is taken by substances which have all the micro-chemical characteristics of lipoids. In the dog the phenomenon affects all liver-cells, which do not, however, appear altered in any other way. In the guinea-pig only a limited number of cells are affected and these become transformed into globoid bodies which are filled with lipoids and are similar to a small number of cells already existing in the liver of healthy and normally fed guinea-pigs. In the liver-cells of the same animals poisoned with phosphorus, neutral fats are found in considerable amount whether the animals are, in addition, kept fasting or not. However, in the liver-cells of dogs poisoned with phosphorus after a period of total fast, both neutral fats and lipoids are seen. Poisoning with phosphorus also causes severe histological and vascular changes of the liver.

C. D. F.

BIOCHEMISTRY

Krause, Dorothy J. The water content of the tissues in experimental beri-beri. *Am. J. Physiol.*, 1922, **60**, 234.

Estimations of the water-content of the tissues of beri-beri chickens, beri-beri pigeons, rats, and guinea-pigs on a beri-beri diet. Only in the beri-beri pigeons, but not in the chickens, rats, and guinea-pigs, the water-content of certain tissues (heart, lungs, skin, muscles, kidneys) was found to be increased. Brain gave an increase in one experiment, a decrease in the other experiment. This is supposed to demonstrate the occurrence of oedema even when it is not in evidence in the usual macroscopic examination.

(Note by Abstractor.—The value of the observations is vitiated by the fact that the figures for the water-content of the few normal controls show enormous variations. The water-content of the skin of normal pigeons is given in the first set of observations on two animals as 41 per cent. and 31 per cent., in the second set as 45 per cent. and 14 per cent., in a third set as 63 per cent. and 62 per cent. In the beri-beri pigeons the figures vary roughly between 60 per cent. and 70 per cent. These latter figures are compared with the figures obtained for the first two sets of observations, so that in beri-beri an increase of over 30 per cent. is found for the water-content of the skin.)

W. C.

Hofmeister, F. Studien über qualitative Unterernährung. I. Die Rattenberiberi. [**Studies on qualitative deficiencies of nutrition. I. Rat beriberi.**] *Biochem. Ztschr.*, 1922, **128**, 540.

In a recent review (*Medical Science*, 1922, **5**, 312) the essential similarity of avian polyneuritis and of beri-beri in man has been questioned. The evidence brought forward by Hofmeister has led him to the view that there is no real difference between the symptoms due to lack of vitamin B in the case of the rat and of the pigeon. This, so far as it goes, bridges the gap between the bird and the mammal, and implies an extension to man. His observations are as follows:

Rats deprived of vitamin B (antineuritic) show four periods of illness—(1) a prodromal stage characterized by loss of appetite, of body-weight, and by a general depression. This stage lasts 29 days; (2) an ataxic stage, in which involuntary movements are badly performed; (3) a stage of spastic condition and involuntary movement followed by (4) a stage of central paralysis leading directly to death. Even as late as stage 3 the animals can be restored to normality by a good dose of the antineuritic vitamin. It is interesting to note that Hofmeister could not find definite peripheral nerve-lesions, characterizable as polyneuritis in his rats. There were found, instead, brain haemorrhages similar to those in chronic alcohol, lead, and arsenic poisoning. Owing to the rapidity with which a vitamin dose restores the normality of the animal, Hofmeister regards the brain purpura as a more or less secondary condition, consequent upon the undernutrition. He regards the whole condition as really due to a lack of nutrition of the functioning elements of the nervous system. This shows itself first in different parts of the nervous system in different animals. In man and the hen peripheral lesions show first, whereas in rats and pigeons the central lesions are the first to appear. Hofmeister considers that the time-honoured argument as to whether the condition is due to deficiency or to toxicity is to a certain extent unreal. It is sufficient to realize that the condition is produced by the undernutrition of a cell and the consequent interference with normal conditions. R. A. P.

Givens, M. H., McClugage, M. B., and van Horne, E. G. The antiscorbutic property of fruits. ii. An experimental study of apples and bananas. *Am. J. Dis. Child.*, 1922, **23**, 226.

Guinea-pigs on a basal diet of soy cake were utilized. Raw apple and banana protect against scurvy. If they are subjected to any considerable temperature treatment, as in preservation by canning or desiccation, a considerable reduction occurs in the antiscorbutic vitamin content.

O. L. V. de W.

Smith, A. H., and Ascham, L. The relation of splenectomy to growth and appetite in the rat. *Am. J. Physiol.*, 1922, **60**, 250.

After splenectomy in rats there was no increase in appetite, no variations in the rate of growth, and no significant alteration in the red-cell count.

W. C.

Sundstroem, E. S. Studies on the adaptation of albino mice to an artificially produced climate. I. Effect on growth and fertility of mice. II. Relation of the body-form and surface area. III. Effect on growth and pigmentation of hair. IV. Effect on resistance of mice to acetonitrile. V. Effect on the blood morphology of mice. *Am. J. Physiol.*, 1922, **60**, 397, 416, 425, 434, 443.

Experiments on a large scale in mice to study the effects of a tropical climate. The various factors considered were temperature, humidity, light, cooling by wind. The experiments extended over several generations of mice.

From the mass of recorded data, which are not all equally convincing, and for which the original papers must be consulted, the following may be quoted as being of special interest.

Exposure to artificial light at ordinary room temperature accelerates the growth of mice. Confinement in a hot and humid atmosphere retards the growth of mice newly transferred to it. Exposure to light in humid heat adds to the retarding effect. Cooling by circulating the hot and humid air neutralizes partly the unfavourable effect of the tropical climate. In mice kept in humid heat the number of red corpuscles was increased, probably owing to a loss of water by the blood. The number of white corpuscles was diminished. W. C.

Burget, G. E., and **Steinberg, M. E. Studies on the physiology of gastro-enterostomy. I. The regurgitation of intestinal contents in normal dogs and dogs with posterior gastro-enterostomy.** *Am. J. Physiol.*, 1922, **60**, 308.

The authors confirm the observations of Boldyreff that the alkaline pancreatic juice and bile are regurgitated into the stomach when the acidity of the gastric contents begins to exceed 0·2 per cent. This reduction in the acidity of the gastric contents regulates the rate at which the stomach empties itself. After posterior gastro-enterostomy the duodenal regurgitation occurs earlier and the stomach empties itself more rapidly. W. C.

Ivy, A. C., and **Whitlow, J. E. The gastric theory put to physiological test.** *Am. J. Physiol.*, 1922, **60**, 578.

The observations on dogs with a gastric pouch failed to give confirmation of the existence of a gastric hormone as postulated by Edkins and Tweedy in their 'gastric theory'. Their results are stated to be due to a lack of adequate controls. W. C.

Lauter, S. Die Abnützungsquote bei Kindern und Schwangern. [**Nitrogen balance in children and pregnant women.**] *Deutsches Arch. f. klin. Med.*, 1922, **139**, 46.

Nitrogen balance experiments with children and women in pregnancy. Lauter finds that the amount of nitrogen necessary to produce a balance in children is low in comparison with their total energy requirements. On the other hand, in pregnant women the ratio is that which is considered to be normal for healthy subjects. C. G. L. W.

Gray, H., and **Edmunds, G. H. Indices of the state of nutrition in children.** *Am. J. Dis. Child.*, 1922, **23**, 226.

A brief review of indices of nutrition, with the application of the different standards to 114 schoolboys. The most satisfactory method hitherto proposed for estimating the correct weight of a normal person, adult or child, is the combination of Dreyer and Hanson's weight-for-stem and weight-for-chest tables. O. L. V. de W.

Gulick, A. A study of weight regulation in the adult human body during over-nutrition. *Am. J. Physiol.*, 1922, **60**, 371.

The paper deals with the interesting and still very obscure problem of the effects of over-nutrition. The particular problem investigated is why a certain type of individual does not put on fat in spite of a high intake of food. The observations were made on the author himself, who represents this type of metabolism, showing a great resistance against fattening. The observations extended over a period of 370 days and record a number of interesting data for which the original must be consulted.

The main facts are that while the basal metabolism, as determined before breakfast in a reclining position, does not rise above the normal, after the intake of food there is some factor at work which causes the fuel food to be burned more freely than in the average individual. This extravagance in oxidation becomes more pronounced during the course of an excessive carbohydrate diet.

The nature of the factor responsible for this extravagant oxidation is not clear. The author excludes thyroid hyperactivity, because the basal metabolism is normal.

(Note by Abstractor.—Although it is true that thyroid hyperactivity of a sufficiently high degree raises the basal metabolism, it does not follow that a normal basal metabolism can be taken as excluding thyroid hyperactivity of a more moderate degree. A significant fact which favours the idea of thyroid hyperactivity, but which the author mentions only casually, is that the respiratory quotient, while fasting 13 hours after a meal, was nearly unity.) W. C.

Trotter, R. T., Edson, P., and **Gesell, R. A comparison of waves of blood-pressure produced by slow and rapid breathing.** *Am. J. Physiol.*, 1922, **60**, 500.

Observations on man with Erlanger's sphygmomanometer on the effects of rapid breathing on blood-pressure. The observations are supplemented by experiments on cats and dogs.

The well-known changes of blood-pressure which occur during a single respiration, and which are complete within the period of a single respiration, are termed 'simple cardio-respiratory waves'. When respiration is rapid cardio-respiratory cycles are established in which the number of respirations is greater by one, or less by one, than the number of heart-beats occurring in the same interval and making up waves of blood-pressure. These are termed 'cardio-respiratory interference waves'. In these, therefore, the length of the wave extends over several respirations. The relation of pulsus alternans is discussed. W. C.

Wieland, H., u. Mayer, R. Pharmakologische Untersuchungen am Atemzentrum. II. Die Beeinflussung des narkotisierten oder morphinisierten Atemzentrums durch Lobelin. [**Pharmacological investigations of the respiratory centre. II. The control of the narcotized respiratory centre by lobeline.**] *Arch. f. exper. Path. u. Pharmakol.*, 1922, **92**, 195.

Lobeline is shown to have a stimulating action on the respiratory centre, in doses of 0·5–1·0 mgm. when administered to rabbits under urethane. The rate of respiration and the volume breathed per minute were both increased. This effect is still produced when the respiratory centre is depressed by morphine or chloral hydrate. There is no mention in the paper of the nicotine-like effect commonly attributed to lobeline, since Edmunds's original description of it. Crystalline lobeline has no paralytic effect on the vagus nerve-endings in the bronchioles, and there is therefore no basis for its use in asthma. J. H. B.

Krzywanek, Fr. W., u. **Steuber, Maria.** Über die Gewinnung der Alveolarluft und die Grösse des schädlichen Raumes beim Hunde. [**The sampling of alveolar air and the volume of the dead space in the dog.**] *Arch. f. d. ges. Physiol.*, 1922, **194**, 477.

A tracheotomized dog accustomed to such experiments breathed through valves, as in the usual Zuntz-Geppert method. Samples of dead-space air were collected at intervals just at the end of expiration by means of a sampling-tube led off from the space between the two valves. The results agreed well; alveolar carbon-dioxide tension was about 35 mm. Hg. and the dead space was about 31 c.cm. (the dog weighed 7·45 kgm.). When the dead space was artificially increased by 13 c.cm., the total reading was also correct, i. e. 44 c.cm. C. L. E.

Haggard, H. W. Studies in carbon monoxide asphyxia. II. The growth of neuroblast in the presence of carbon monoxide.] *Am. J. Physiol.*, 1922, **60**, 244.

By experiments on *in vitro* cultures it was shown that carbon monoxide by itself has no ill effect upon growing nerve-cells, even in concentrations of 79 per cent. It is in this respect as neutral as nitrogen. Its toxic action on the body as a whole is due solely to the asphyxia resulting from its combination with haemoglobin. Illuminating gas, however, contains, in addition to carbon monoxide, another toxic substance, for it is toxic to neuroblast cultures in concentration of as little as 0·1 per cent.

It is specially stated that this observation is not to be interpreted as weighing against the view that the toxicity of illuminating gas on the entire organism is due to the carbon monoxide and the asphyxia which it produces. W. C.

Starlinger, W. Ueber die physikalisch-chemische Beeinflussung des Blutes durch Tuberculin, gemessen an der Suspensionsstabilität der Erythrocyten und dem Flockungsvermögen des Plasmas. [**The physico-chemical influence of tuberculin on the stability of blood suspension and the agglutination of the plasma.**] *Ztschr. f. d. ges. Exper. Med.*, 1922, **27**, 305.

The author takes up the very important question as to whether the injection of a substance like tuberculin produces changes in the blood which are of a physico-chemical nature. This question has been investigated without entirely satisfactory conclusions by Izar, Csepai and Torday, Obermayer and Pick, and by Abderhalden. In the present study the author has utilized the sedimenting properties of blood and the 'flocking' in healthy and tubercular patients through tuberculin A. T. K. Tuberculin has the property of inhibiting the agglutination and sedimentation of erythrocytes and of preventing agglutination, but this stabilizing action only occurs when the two mixtures are in short contact with one another. The process appears to be due to a combination of the coarsely dispersed protein colloids with the components of the bodies of the tubercle bacillus. As this occurs both in tubercular and non-tubercular subjects it cannot be looked upon as having a specific character. C. G. L. W.

Feil, H., and **Forward, D. D. The pulse in the portal vein.** *Am. J. Physiol.*, 1922, **60**, 312.

Records of the portal pulse in dogs and interpretation of the factors which determine the portal pulse. W. C.

Martin, K. A., and **White, H. L. Blood-pressure responses to hypersystolic compression of tissues.** *Am. J. Physiol.*, 1922, **60**, 323.

Lasting compression of the forearm great enough to produce a local ischaemia produces after 15–45 minutes a rise in systolic and diastolic arterial pressures tending to exceed the compressing pressure. The rise is maintained for at least 60 minutes. It appears earlier with smoking than without. It is accompanied by headache, sweating, and a sensation of heat. In smoking there is also nausea, even with habitual smokers. The rise is probably due to splanchnic vasoconstriction. When the compression is released the blood-pressure returns to its normal level: it may even fall below it and then there are symptoms of collapse.

The authors believe that there is probably a connexion between these results and the mechanism of certain types of clinical hypertension.

W. C.

Evans, C. L. Acid production in shed blood. *J. Physiol.*, 1922, **56**, 146.

The fall in carbon dioxide capacity of shed blood, first observed by Zuntz, is due to a conversion of glucose into lactic acid. This change is accelerated by a lowering of the CO_2 pressure of the blood, and can be retarded by adding 0·05 to 0·1 per cent. sodium fluoride. Equilibrations at body-temperature can then be performed with little change in the CO_2 capacity of the blood. O. L. V. de W.

Barcroft, J., Bock, A. V., Hill, A. V., Parsons, W., Parsons, T. R., and **Shoji, R. On the hydrogen-ion concentration and some related properties of normal human blood.** *J. Physiol.*, 1922, **56**, 157.

Relations have been established experimentally at 37° C. between plasma CH and CO_2 pressure, between CO_2 pressure and volume per cent. absorbed CO_2, between volume per cent. of absorbed CO_2 and the H-ion concentration: also between 1/K and CO_2 pressure, K being the constant of Hill's equation, and between 1/K and CH. O. L. V. de W.

Dale, H. H., and **Evans, C. L. Effect on the circulation of changes in the carbon dioxide content of the blood.** *J. Physiol.*, 1922, **56**, 125.

Excessive rapid artificial respiration in the cat produces a sudden fall in the arterial blood-pressure of 30 to 40 mm. Hg. The resumption of a slow rate of artificial respiration leads to a rapid restoration of the blood-pressure to its original level. A similar result ensues if ordinary human expired air is substituted for pure air, while rapid artificial respiration is continued. It is found that these effects are due to depression and recovery of the vasomotor centres of the bulb and cord: that they are the result of

abstraction and replacement of free carbon dioxide, and not due to the change of P_H towards the alkaline side, which results from the forced respiration.
O. L. V. de W.

Löhr, H. Die Beeinflussung der Blutkörperchensenkungsgeschwindigkeit durch Reizstoffe. [**The influence of protein stimulant injection on the rate of blood sedimentation.**] *Ztschr. f. d. ges. exper. Med.*, 1922, **27**, 1.

The rate of sedimentation of red blood-cells is increased by various kinds of stimulants, and the effect is seen in one hour if these substances are administered intravenously. There is a strong parallelism between increase in sedimentation rate and the rise in typhoid agglutinins after the administration of stimulants.
C. G. L. W.

Kiyotaki, U. Nephelometrische Studien über den Einfluss der Temperaturerhöhung auf Serum und Plasma. [**Nephelometric studies on the influence of a rise of temperature upon serum and plasma.**] *Biochem. Ztschr.*, 1922, **128**, 354.

Nephelometric observations show that a cloudiness develops in serum upon heating. This occurs most rapidly at 45–46° C., but is marked over the fever range 39–42° C. The author thinks that this latter fact may explain the changed conditions of the body proteins in fever. The heated serum did not behave abnormally towards the complement of fresh guinea-pigs' serum.
R. A. P.

Gad Andresen, K. L. A micro-method for the estimation of ammonia in blood and organic fluids. A micro-urease method for the estimation of urea in blood, secretions, and tissues. *J. Biol. Chem.*, 1922, **51**, 367, 373.

Folin, O. A system of blood analysis. A new colorimetric method for the determination of the amino-acid nitrogen of blood. A colorimetric determination of the amino-acid nitrogen in normal urine. Colorimetric methods for the separate determination of tyrosine, tryptophane, and cystine in proteins. *J. Biol. Chem.*, 1922, **51**, 377, 393, 421.

The titles of the papers on micro-methods of estimation explain themselves. The method developed by Otto Folin for the colorimetric estimation of amino-acid nitrogen in blood is quite new. He has employed for this purpose the sodium salt of β-naphthaquinone sulphonic acid. He has further been able to extend his estimation to the quantitative determination of tyrosine, cystine, and tryptophane. It is interesting to note that the amount of tryptophane found in casein, namely, 1·54, agrees closely with the figure found by Hopkins and Cole by gravimetric methods.
R. A. P.

Wiechmann, E. Weitere Untersuchungen über die Durchlässigkeit der menschlichen roten Blutkörperchen. [**Further investigations on the permeability of human red blood corpuscles.**] *Arch. f. d. ges. Physiol.*, 1922, **194**, 435.

The permeability of red cells to sulphonic acid dyes, such as cyanol, Lichtgrün FS, Setopalin, and Ponceau 2 R, is not altered by removal of carbon dioxide from the blood, or by saturating the blood with pure carbon dioxide. In this respect there is a difference from the inorganic SO_4 ion, which shows an ionic interchange between corpuscle and plasma under similar conditions. The permeability for bromides, and the tendency to laking by hypotonic solutions of salts, were both reduced by digifolin and strophanthin. C. L. E.

Anrep, G. V., and **Cannan, R. K. The metabolism of the salivary glands. Blood-sugar metabolism of the submaxillary gland.** *J. Physiol.*, 1922, **56**, 248.

Various possible causes of the disappearance of glucose from blood passing through the salivary gland are discussed. No sugar could be demonstrated in the saliva. The lymph flow was calculated from the haemoglobin ratio of arterial and venous blood of the gland, and its sugar content assumed to be equal to that of the plasma. Any glycogen storage was regarded as 'consumption' of sugar. The mean sugar consumption of the resting gland amounted to 2·07 mgm. per gm. per hour. This agrees well with Barcroft's estimation of consumption of oxygen by the resting gland, which, if the substance oxidized is assumed to be glucose, would give a consumption of 1·8 mgm. per gm. per hour. Atropine has no effect on the sugar consumption of the resting gland. Pilocarpine increases the blood-sugar consumption, the increase being within broad limits proportional to the salivary flow. The increase per c.cm. of saliva secreted varied from 0·7 to 2·7 mgm. O. L. V. de W.

Wilder, R. M., Boothby, W. M., and **Beeler, C. Studies on the metabolism of diabetes.** *J. Biol. Chem.*, 1922, **51**, 311.

In this paper a complete metabolic study of a fatal case of diabetes is recorded. The case is one of a female subject with no previous history of illness or of family predisposition to the disease. Diabetes arose abruptly in the 28th year and lasted for 2 years 11 months until death in coma. Altogether the case was studied for 74 days, 11 different variants of the diet being tried. The respiratory quotient remained fairly constant at 0·69, giving no ground for the belief that carbohydrate was being utilized. The basal metabolic level was considerably lower than the normal, though its depression was controlled to a certain extent by the amount of food taken. Protein especially caused a rise in the level of basal metabolism persisting for some time and analogous to the specific dynamic action of protein found in metabolic studies. The critical or fatal D. N. ratio (3·65) occurred most readily upon a high protein diet. It was clear that, although the high caloric diet tended to aggravate the disease, the sugar tolerance was much more depressed by protein than by iso-caloric amounts of food. An unexplained new observation was a depression of the respiratory quotient after the taking of food.

A dangerous rise of acidosis was checked upon two occasions by administration of a diet containing 2 gm. molecules of fatty acid to 1 gm. molecule of glucose. The calculated ratios of ketogenic to antiketogenic substances for two days upon which the acidosis was minimal were 1·5 : 1 and 1·8 : 1. In connexion with this, the view held by Woodyatt and Shaffer that the balance of ketogenic to antiketogenic substances in the diet should be in the ratio of 1 : 1 is not borne out completely by this case, which indicates that a ratio of 2 : 1 may prevent the appearance of acidosis. A careful study of this nature is clearly of considerable importance for the advance of accurate knowledge of diabetes. R. A. P.

Allen, F. M. **The pathology of diabetes. 6. Pancreatitis in the aetiology of experimental diabetes. 7. Microscopic studies of the pancreas in clinical diabetes. 9. Literature and discussion.** *J. Metabol. Res.*, 1922, **1**, 165, 193, 251.

The difference between human diabetes and that produced experimentally in the dog is due, in large part, to the fact that in the diabetic pancreas there is always evidence of a long-standing previous damage, and the visible changes do not give an accurate measure, in a diabetogenic sense, of the real abnormalities of the organ. The consequences of acute inflammation are rarely progressive in dogs, and the resulting diabetes is subject to dietary control like that following simple partial pancreatectomy. Whatever acute injuries the islands sustain, their subsequent preservation or destruction depends upon the diet and the occurrence or non-occurrence of hydropic degeneration. In the seventh paper of this series it is shown that the pancreas in every case of diabetes has borne marks of infectious or toxic damage. Hydropic degeneration is demonstrated in the human pancreas whenever diabetic symptoms have been sufficiently intense and prolonged. It is ordinarily missed in the mildest cases and is to be interpreted as an anatomical breakdown of the island cells by over-stimulation of their internal secretory functions on excessive diet. The pathological findings give the impression that 'from the standpoint of primary aetiology the diabetic pancreas in most cases represents a burn-out conflagration, and the chief or sole cause of aggravation of the condition lies in hydropic degeneration of islands'. This interpretation alters the former conception of diabetes as an inherently progressive disease, and affords grounds for regarding the average case as the consequences of damage of a vital organ which is in danger of further injury chiefly or solely from functional overstrain. Clinical evidence to date corroborates this view by showing that by sufficient dietary control the downward progress of most cases of diabetes is either halted or almost indefinitely delayed. In the ninth paper a *résumé* of Allen's work and a critical survey of the literature is given.

C. G. L. W.

Allen, F. M., and **Wishart, M. B.** **Alcohol in the diabetic diet.** *J. Metabol. Res.*, 1922, **1**, 281.

A critical review of the literature on the use of alcohol in diabetic diets is given and experiments detailed of its use in two cases of diabetes. Alcohol is not converted into sugar or into acetone and can be used to replace food in the diet, but as the treatment of diabetes is essentially one of under-nutrition its use is not indicated. It does not prevent the onset of coma. If added to a diet which is sufficient just to prevent the appearance of sugar in the urine it produces a return of glycosuria and other symptoms. 'The most important lesson, however, is that all attempts to find some special or synthetic food which the diabetic shall be able to metabolize so as to restore normal nutrition without excretion of sugar or acetone are forever impossible. This limitation . . . can only be removed by a cure which shall supply the missing product of the pancreas.'

C. G. L. W.

Leclercq, F. S. Over-nutrition with fat and alcohol in severe diabetes. *J. Metabol. Res.*, 1922, **1**, 307.

Experiments on two patients with severe diabetes demonstrated the production of hyperglycaemia in consequence of adding excessive calories to the diet in the form of either fat or alcohol. C. G. L. W.

Moraczewski, W. Diagnostische Bedeutung der Wasserprobe bei Nierenkranken. [**The diagnostic importance of the water test in kidney disease.**] *Ztschr. f. d. ges. exper. Med.*, 1922, **27**, 265.

The author has investigated two points in the excretion of water by the kidney:

(1) Whether the water test performed at intervals gives some idea of the prognosis in a case of renal disease, and (2) whether one may estimate the efficiency of diuretics by their action in the water test, and possibly choose a suitable drug for a specific case.

The drugs investigated were calcium chloride, urea, caffeine, potassium acetate, theobromine, theophylline, digitalis, urotropine, &c. Curves are given for various diuretics compared with a similar diuresis induced by 1,000 c.cm. of weak tea. In some of the cases the patient came to post-mortem and the changes in the kidneys were controlled in this way. The sclerotic kidney is indicated by a late elimination, practically no urine being excreted in the first half-hour. Cases of glomerulonephritis and mixed nephritis tending to recovery give the picture of a normal kidney. Light cases of nephritis without albumin give a delayed but copious urinary excretion. On a thirsting diet diuretics provoke early excretion both in healthy and in diseased kidneys, and the maximum amount of urine is excreted later when the amount of fluid is greater. Diuretics appear to have more effect upon the diseased kidney than on one which is in a normal condition. C. G. L. W.

Folin, O., and **Berglund, H. The retention and distribution of amino-acids, with especial reference to the urea formation.** *J. Biol. Chem.*, 1922, **51**, 395.

The problem investigated in this paper concerns the part played by the liver in the formation of urea from amino-acids. The older conception was that amino-acids taken to the liver were de-aminated there. The new methods of analysis of amino-acids developed by Folin have given the opportunity of testing this problem. If it can be shown that during the absorption of small amounts of amino-acids after a meal there is a rise in the amino-acid content of the plasma previous to the rise in urea content, it is clear that the amino-acids are in large part reaching the tissues. The results obtained show that there is 100 per cent. increase in the amino-acid nitrogen of the blood previous to any increase in the urea content of the same. After about two hours the urea formation begins to increase and the amino-acid amount to subside. This seems to indicate once more that the liver only plays its part in the general story of the de-amination of amino-acids. Other interesting figures dealing with the amino-acid nitrogen of the urine are also given in this paper. R. A. P.

Barrenscheen, H. K. Über Fructosuria. [**On fructosuria.**] *Biochem. Ztschr.*, 1922, **127**, 222.

A case of fructosuria is described, in which there is a family history of diabetes. On the father's side, the brother of the grandfather, the father, and the father's brother had diabetes. The mother's side had gout and morbid obesity.

The amount of fructose split off was shown to depend upon alimentary influences. Giving fructose by the mouth led to a large increase in the amount of sugar in the blood, which fell in the course of two hours with appearance of fructose in the urine. The author discusses the part played by the liver, viz. the view that in these cases there is a loss of power to make glycogen from fructose. R. A. P.

Clark, G. A. Glucose absorption in the renal tubules of the frog. *J. Physiol.*, 1922, **56**, 201.

The normal plasma sugar of the frog is 0·045 per cent. If both aorta and renal portal vein are perfused with a perfusing fluid containing the same percentage of glucose, no sugar appears in the urine if less than 0·052 per cent. is present in the perfusing fluid. With a glucose content above this 'threshold' but less than 0·23 per cent., the concentration in the urine was less by 0·05 to 0·03 per cent. than that of the perfusing fluid; with concentrations above 0·23 per cent. the whole of the sugar escapes. If the renal arteries are perfused with a fluid containing less than 0·1 per cent. glucose, and the renal portal veins with a fluid containing 0·4 to 0·5 per cent. at half the pressure, when the mixed perfusate contains 0·21 per cent. glucose and upwards, the kidney is completely permeable to the sugar of the arterial perfusate. Since no sugar passes through the tubular epithelium, and since the renal portal transfusion does not reach the glomerulus, the only possible conclusion is that under these conditions the glucose filtered through the glomerulus is no longer absorbed by the tubules. Re-absorption is only possible if the capillaries surrounding the tubules contain glucose at a concentration less than ten times that normally present in the blood. The glomerular membrane is completely permeable to glucose, even with concentrations in the arterial perfusing fluid as low as 0·01 per cent. Calcium is necessary for the normal activity of the tubule.

O. L. V. de W.

O'Connor, J. M., and **Conway, E. J. Localization of excretion in the uriniferous tubule.** *J. Physiol.*, 1922, **56**, 190.

If all substances pass through the glomerulus, the urine will only show an increased concentration of a substance injected into the bloodstream when the contents of the dead space—ureter, renal pelvis, collecting tubules, and uriniferous tubules have been expelled. The authors attempt to calculate this dead space in the rabbit, and conclude from experiments that iodide is excreted through the glomerulus, uric acid by the second convoluted tubules, and sodium chloride sometimes by the tubule, sometimes through the glomerulus. O. L. V. de W.

Röckemann, W. Über Tetralinharn. [**The urine after administration of tetraline.**] *Arch. f. exper. Path. u. Pharmakol.*, 1922, **92**, 52.

When tetrahydronaphthaline (tetraline) is fed to a dog, it is oxidized and appears in the urine as ac-α-tetralol, while in the rabbit it appears as ac-β-tetralol, and is excreted combined with glycuronic acid. It is interesting that the ac-β-tetralol is dextro-rotatory. J. H. B.

Starkenstein, E. Über die pharmakologische Beeinflussung der Nierenfunktion. [**On the pharmacological control of kidney function.**] *Arch. f. exper. Path. u. Pharmakol.*, 1922, **92**, 339.

When administered to rabbits, dogs, or human beings, atophan has no diuretic effect. Adrenalin, after subcutaneous injection, produces glycosuria and a slight diuresis. If atophan be injected before adrenalin, then there is a large diuresis. A similar large diuresis is caused by atophan (*a*) when glucose solution is injected intravenously, (*b*) when NaCl solution is injected intravenously. J. H. B.

Bakwin, H. The significance of hydremia in the secretion of urine. *Am. J. Physiol.*, 1922, **60**, 343.

In healthy infants the concentration of the blood and of the urine were studied after drinking of water and after saline. After water there was a hydraemia, but no diuresis. After saline there was a hydraemia, which was slightly more marked than after water, and an oliguria. In infants, then, hydraemia does not necessarily cause diuresis. W. C.

Amberg, S., and **Mayer, M. E. The isolation of a substance from urine having properties of citric acid.** *Am. J. Physiol.*, 1922, **60**, 564.

A substance was isolated from human urine which gave all the reactions of citric acid. It occurs in very small quantities. It was isolated in the form of an impure barium salt. The interest of this observation lies in finding that a readily oxidizable organic substance such as citric acid should be normally excreted in the urine. W. C.

Cannon, W. B., and **Smith, E. P. Studies on the conditions of activity in endocrine glands. IX. Further evidence of nervous control of thyroid secretion.** *Am. J. Physiol.*, 1922, **60**, 476.

Confirmation of previous work by Cannon and his co-workers that the thyroid is innervated by the sympathetic and that activity of the gland by stimulation of the cervical sympathetic or massage of the gland causes an increased rate of the denervated heart, indicating that the thyroid hormone stimulates the sympathetic. This effect on the heart is slow, requiring from 30–60 minutes to appear, and passes off in a similarly slow manner. It differs in that respect from the action of adrenalin and the effect can be produced in the absence of the adrenal glands. Asphyxia and stimulation of afferent nerves produce secretion of the thyroid hormone. In an addendum it is stated that the observation when repeated in March and April gave negative results. This is attributed to the fact that the thyroid at the end of the winter contains a greatly reduced amount of its specific hormone as compared with the summer. W. C.

Cannon, W. B., and **Griffith, F. B. Studies on the conditions of activity of the endocrine glands. X. The cardio-accelerator substance produced by hepatic stimulation.** *Am. J. Physiol.*, 1922, **60**, 544.

When the hepatic nerves (splanchnics) are stimulated a substance is discharged from the liver into the blood-stream, which raises the blood-pressure and accelerates the rate of the denervated heart. Its action resembles therefore that of adrenalin: it is sympatho-mimetic. A study of the action of the known products of hyperactivity (amino-acids, bile, urea, glucose, &c.) showed that this action could not be attributed to them, so that the substance must be assumed to be of a special and unknown nature. It is suggested that it may be related to the protein granules observed in the liver-cells by Berg and found by Hübel to be discharged by adrenalin. The authors refrain from classing this substance as a new internal secretion.
W. C.

Fornet, B. Studien über die Gefässwirkung des Adrenalins beim Menschen. [**Studies on the effect of adrenalin on the vessels in human subjects.**] *Arch. f. exper. Path. u. Pharmakol.*, 1922, **92**, 165.

The author has investigated the destruction of adrenalin when administered to hospital patients. If a ligature be placed tightly round the arm and 0·05 mgm. adrenalin be injected intravenously below the ligature, then, even if the ligature is not removed until ten minutes after the injection, the removal is followed by a large rise of blood-pressure. He concludes that the view that adrenalin is rapidly destroyed in the blood is wrong. He also shows that there is a considerable effect on the blood-pressure, when it is injected subcutaneously. J. H. B.

Rapport, E. Studies in experimental traumatic shock. VI. The liberation of epinephrin in traumatic shock. *Am. J. Physiol.*, 1922, **60**, 461.

Confirmation of the observations of Bedford and Jackson and of Cramer, that there is over-secretion of adrenalin in traumatic shock, and that neither over-secretion nor exhaustion of the adrenals is a factor in the production of shock. It is suggested that the over-activity of the glands is a conserving factor tending to protect the organism against the consequences of shock.
W. C.

Hartmann, F. A., Waite, R. H., and **Powell, E. F. The relation of the adrenals to fatigue.** *Am. J. Physiol.*, 1922, **60**, 255.

In cats one adrenal was removed, the other was denervated so that the output of epinephrin was greatly diminished. Such cats often show a period of ill health, indicated by loss of appetite, loss of weight, change of temperament, weakness, and sometimes a subnormal temperature. Their capacity for muscular work is diminished. Observations on normal cats doing muscular work show that an increased resistance to fatigue is associated with an increased output of adrenalin, as indicated by the denervated pupil reaction.

Adrenalin plays, therefore, an important part in increasing the capacity for muscular work and delaying the onset of fatigue. W. C.

Ulrich, H. L., and **Rypins, H. A note on adrenalin hyperglycaemia in man.** *J. Pharmacol. & Exper. Therap.*, 1922, **19**, 215.

The mechanism of adrenalin hyperglycaemia in man cannot be explained on the basis of a change in blood concentration due to the drug, but occurs independently of such a change. Adrenalin causes a wide and inconstant fluctuation in the concentration of blood creatinin and blood urea nitrogen.
C. G. L. W.

Winter, L. B., and **Smith, W. Formation and distribution of phosphates in muscle.** *J. Physiol.*, 1922, **56**, 227.

Some modifications are described in the method for localizing phosphorus in tissues microscopically. It is found that the uncombined phosphate in striated muscle is increased in vigour. No such increase occurs in unstriated muscle. O. L. V. de W.

Schott, A. Die chemische Contractur des Säugetiermuskels bei erhaltener und fehlender 'elektrischer Erregbarkeit'. [**The chemical contracture of mammalian muscle when the electrical excitability is retained or lost.**] *Arch. f. d. ges. Physiol*, 1922, **194**, 271.

The effects of chloroform, n/50 sodium hydroxide, and n/100 hydrochloric acid (all in Ringer's solution), were compared on fresh excitable muscle, and on muscle the excitability of which had been lost as a result of cold, heat, or conservation. When muscle was cooled, there was often some shortening during the cooling. Chloroform and sodium hydroxide, at all temperatures, caused chemical contracture, even when the muscle was electrically inexcitable; at the higher temperatures the contracture was greater and of more sudden onset than at the lower. Hydrochloric acid was ineffective at low temperatures (1–5°), but caused the usual contracture at room temperature. After long conservation the effect was less, even though the muscle was still electrically excitable. Chloroform rigor could always be resolved by hydrochloric acid, and sometimes by sodium hydroxide. Some of these facts are opposed to the view that the stimulating substance in muscular contraction is invariably an acid. C. L. E.

Clover, A. M. The auto-oxidation of ethyl ether. *J. Am. Chem. Soc.*, 1922, **44**, 1107.

When a glass-stoppered bottle containing ordinary ethyl ether is allowed to stand for several months and the ether is allowed to evaporate, a liquid residue remains which possesses a very pungent odour and oxidizing properties. This is due to the absorption of oxygen from the air with the formation of a peroxide by direct addition. The peroxide decomposes, forming acetic aldehyde, and this compound greatly accelerates the peroxide formation. The author has been able to isolate sufficient ether peroxide from ether which has stood in light and air to be able to study its properties and decomposition products. C. G. L. W.

Hildebrandt, F. Über Veränderungen des Stoffwechsels nach chronischer Morphinzufuhr. [**On the metabolic changes following chronic morphine poisoning.**] *Arch. f. exper. Path. u. Pharmakol.*, 1922, **92**, 68.

In the first place the author has carried out some interesting and careful experiments on the metabolism of rats (*a*) when fed with thyroid gland, (*b*) when thyroidectomized. He measures the oxygen intake and CO_2 production in rats by E. Rohde's method during five consecutive one-hour periods after the consumption of a standard meal. He also estimates their excretion of nitrogen. In this way he establishes that feeding with thyroid (1) increases the oxygen consumption, (2) increases the N excretion, (3) lowers the respiratory quotient. In the first week or two following thyroidectomy, on the other hand, he finds that, compared with the rat before the operation, (1) the oxygen consumption is diminished, (2) the respiratory quotient rises to the neighbourhood of 1·0. He concludes, from the changes in the respiratory quotient, that feeding thyroid gland increases the proportion of fat metabolized, while removal of the thyroid gland diminishes the combustion of fat. The result of the continued administration of morphine to rats over a period of 28 days (in which daily doses were increased from 10 mgm. per 100 gm. to 60 mgm. per 100 gm.) was to change the metabolism in the same way as did thyroidectomy, and the respiratory quotient rose from 0·7 or 0·8 to 0·9 or 1·0. J. H. B.

ABDERHALDEN, E., u. SCHIFFMANN, OLGA. Weitere Untersuchungen über die von einzelnen Organen hervorgebrachten Substanzen mit spezifischer Wirkung. VII. [**Further investigations on the substances with specific action formed by organs. VII.**] *Arch. f. d. ges. Physiol.*, 1922, **194**, 206.

Chemotactic experiments on *Paramoecia* and observations on the rate of multiplication were made under the influence of various 'optones'. Corpus luteum, pituitary, ovary, thyroid, and thymus optones, in dilutions of 1 per cent., were lethal or negatively chemotactic, though higher dilutions were positively chemotactic. Thymus, testis, and thyroid accelerated, while pituitary and corpus luteum inhibited, division. C. L. E.

PRIGGE, R. Die Wirkung der intravenösen Zufuhr grosser NaCl-Mengen bei Pneumonie und beim Gesunden. [**The action of large quantities of salt solution injected intravenously in pneumonic and healthy subjects.**] *Deutsches Arch. f. klin. Med.*, 1922, **139**, 1.

The question of the well-known retention of sodium chloride during pneumonia has been investigated by the author, who comes to the following results. If large quantities (20-38 gm.) of highly concentrated sodium chloride solution are injected intravenously they disappear from the circulation without appearing in the urine. In healthy subjects the salt is eliminated by the kidneys in about 2 days. In pneumonia the salt is retained and does not appear in the urine during the whole course of the disease The hyperchloraemia which is seen at the beginning of the injection is of short duration both in normal and in pneumonic subjects. If one speaks of the ratio of the weight of plasma to the weight of blood corpuscles as the 'hydraemic index', then in all cases where sodium chloride has been injected this index rises. This is due to a transference of fluid from the tissues to the circulatory system, and also is in part due to a giving up of fluid by the erythrocytes themselves. By suitable technique injections of large concentrated salt solutions produce no ill effect, and in certain cases, where low blood-pressure are present, is indicated in order to raise the same.

C. G. L. W.

Kojima, K. Über den Chemismus der Toxinbildung durch den Bac. phlegm. emphys. Fränkel. [**Upon the chemistry of toxin formation by *B. phlegmonae emphysematosus.*]** *Biochem. Ztschr.*, 1922, **128**, 519.

This is an interesting illustration of the fact that the conditions of nutrition may profoundly modify the toxicity of a bacterial strain. The Fränkel bacillus produces two poisons, an acute one which kills immediately, and one which kills after a definite incubation period. When there is more than 0·5 per cent. of cane sugar in the medium the acute form of toxin is produced; when the amount of sugar is less the slower-acting toxin arises. Other differences appear between the two poisons, the acute one being thermostable, and not capable of neutralization with Fränkel serum, whereas the other is thermolabile and can be neutralized by Fränkel serum.

R. A. P.

de Wesselow, O. L. V. Some chemical observations on the toxaemias of pregnancy. *J. Obst. & Gynaec. Brit. Emp.*, 1922, **29**, 21.

The author has examined a number of albuminuric and eclamptic cases of pregnancy, and has controlled his results by the examination of a number of normal pregnancies. He has investigated the urea and non-protein nitrogen of the blood, the fibrinogen nitrogen and lipase of the plasma, the nitrogen partition of the urine, the diastatic index, and has tested the renal efficiency of these patients. He gives a critical review of the information which is available on the testing of the hepatic function as an index of the condition in pregnancy. As a result of this work he does not believe that one can detect the presence of a liver lesion in these cases, and no evidence was obtained by the methods employed of a differentiation into groups, nor were there any chemical differences observed between those cases which were prolonged by convulsions and those in which no convulsions occurred. On the other hand, he believes a chemical examination can be of definite value in averting the risk of permanent damage to the mother and to indicate the stage at which induction becomes necessary. The definitely raised urea content of the blood above 40 mgm. per 100 c.cm. is proof that the kidney is severely damaged and is an indication for induction. The urea concentration test affords evidence of the condition of the renal function, and when the figure is below 2 per cent. termination of the pregnancy should be considered. The rise in blood urea with a falling concentration capacity constitutes an obvious indication of a progressive lesion. In all cases, blood-pressure observations afford most valuable assistance in prognosis and treatment.

C. G. L. W.

Gunn, J. W. C., and Goldberg, M. The action of salicylates on the uterus. *J. Pharmacol. & Exper. Therap.*, 1922, **19**, 207.

It has been suggested that abortion sometimes occurs during the treatment of acute rheumatism with salicylates. It is found that sodium salicylate has a stimulating action on the uterus, but only in concentrations higher than those found in the blood during the treatment of rheumatic fever. It is suggested that in these cases the abortion is the result of fever, and that salicylates have little effect unless the uterus is especially sensitive.

C. G. L. W.

Langer, H. Die Grundlagen der biologischen Desinfektionsleistung von Acridiniumfarbstoffen, insbesondere von Flavocid. [**The biological basis of the disinfectant action of acridine dyes, especially of flavacid.**] *Ztschr. f. d. ges. exper. Med.*, 1922, **27**, 174.

The members of the acridine group, to which flavine belongs, show differences in their bactericidal power corresponding to their dispersion. A lessening of the dispersion increases their action, and the increase in disinfectant activity by the addition of serum is due to this. Alkali acts in the same way. The disinfectant action is greater with Gram-positive bacteria than with Gram-negative. It is greatest with the pus-forming group and with *B. diphtheriae.* While these dyes give rise to local action, when administered subcutaneously, they are without effect when injected intravenously in doses of 1 to 3 mgm. per kilo. C. G. L. W.

Schittenhelm, A., u. **Harpuder, K.** Resorption und bakterielle Zersetzung der Purinsubstanzen im Darmkanal von Mensch und Tier. [**Resorption and bacterial decomposition of purins in the intestinal tract in men and animals.**] *Ztschr. f. d. ges. exper. Med.*, 1922, **27**, 29.

Nucleins given by the mouth are quickly absorbed in the intestinal tract after being broken up into their component parts. Only a small portion reaches the large intestine. C. G. L. W.

Schittenhelm, A., u. **Harpuder, K.** Über das Schicksal gehäuft injizierter Harnsäure beim Menschén. [**The fate of injected uric acid in man.**] *Ztschr. f. d. ges. exper. Med.*, 1922, **27**, 34.

After the administration of an excess of uric acid only a small part of substance is found in the urine or in the organs. C. G. L. W.

Bürger, M., u. **Grauhan, M.** Über post-operativen Eiweisszerfall. [**Post-operative protein breakdown.**] *Ztschr. f. d. ges. exper. Med.*, 1922, **27**, 97.

The authors have utilized the antitryptic titre of the serum to investigate where this stands in relation to tissue damage. They show that processes connected with damage to the tissue lead to the appearance of substances in the blood which inhibit tryptic digestion *in vitro.* They do not believe that this action is due to an antiferment, but to an excess of protein breakdown products, and believe that a fall in the antitryptic titre is of good prognostic significance. They look on wound shock as partly a proteinogenic cachexia and believe that every effort should be made to remove the toxic decomposition products if improvement is to be obtained.
C. G. L. W.

Jarisch, A. Beiträge zur Pharmakologie der Lipoide. II. Seife und Serum. [**Contributions to the pharmacology of the lipoids. II. Soaps and Serum.**] *Arch. f. d. ges. Physiol.*, 1922, **194**, 337.

Soaps are hydrolysed by serum, the fatty acids set free combining with the proteins of the serum to give a clear solution from which they are not precipitated either by calcium chloride or by acids. After removal of salts from the serum by dialysis, the addition of soaps, colloidal fatty acids, alcoholic organ extracts, cholesterol, commercial lecithin, saponin, bile, sodium desoxycholate, thymol, camphor, tributyrin. or various narcotics, yields a voluminous precipitate, apparently of globulin. The resistance to hypotonic solutions, produced by the addition of soap to red cells, is also seen in serum and is due to the formation of protein-fatty acid combinations. The lowering of resistance to haemolysis of red cells, produced by washing in physiological salt solutions, is due to the action of carbon dioxide contained in such solutions, and is not seen if the saline is carbon-dioxide free. Sodium bicarbonate raises the resistance of red cells to hypotony, and lowers that to heat, while also favouring flocculation of the stroma substance. C. L. E.

Tashiro, S. Studies on alkaligenesis in tissues. I. Ammonia production in the nerve during excitation. *Am. J. Physiol.*, 1922, **60**, 519.

Methods are described by which the most minute amounts of ammonia can be determined—as little as one-millionth of a gramme. The author claims to have shown that resting nerve gives off very small amounts of a volatile base-forming substance, which is probably ammonia. The liberation of this substance is increased when the nerve is stimulated. W. C.

Freudenberg, E., u. **Gyorgy, P.** Über Kalkbindung durch tierische Gewebe VII und VIII. [**On the calcium combination with animal tissues.**] *Biochem. Ztschr.*, 1922, **129**, 134, 138.

These two papers represent part of a systematic attempt to investigate the mechanism of the combination of calcium with cartilage tissue. It is found that cartilage takes up less calcium from solutions of calcium chloride than from solutions of calcium acetate, nitrate, phosphate, and bicarbonate. Creatin and ethylamine inhibit the taking up of calcium by cartilage; so do formaldehyde and glucose. Ethyl alcohol and acetone have no effect.

In connexion with work of this type it must be remembered that it has recently been shown that in the absence of the fat-soluble A vitamin ossification does not proceed normally. R. A. P.

Bayer, G. Über den Calciumgehalt des Blutes bei der Guanidinvergiftung. Ein Beitrag zur Tetaniefrage. [**The calcium content of the blood in guanidine poisoning. A contribution to the study of tetany.**] *Ztschr. f. d. ges. exper. Med.*, 1922, **27**, 119.

In an investigation of some points in the aetiology of parathyroid tetany it was found that poisoning with guanidine results in a speedy lessening of the amount of calcium ions in the serum. This, however, is not so great as occurs after parathyroidectomy. It is suggested that the poison acts upon the epithelial bodies and overstrains them in their attempt to convert it into creatinin. They are, therefore, unable to fulfil their normal functions. C. G. L. W.

RADIOLOGY AND ELECTROLOGY

Radiobiology

Lin, J. H., Sturm, E., and **Murphy, J. B. Studies on X-ray effects. XI. The fate of cancer grafts implanted in subcutaneous tissue previously exposed to X-rays.** [**B.**] *J. Exper. M.*, 1922, **35**, 487.

Attention is called to the fact that an erythema dose of X-rays renders the area refractory to subsequent intracutaneous inoculation of cancer, but not to subcutaneous inoculation. The paper deals with the question as to whether or no direct irradiation of the deeper tissues renders them refractory to cancer inoculation. Experiments were carried out on white mice, a flap of skin over the abdomen being reflected and irradiated: details of the experiment are fully described. From this experiment it was found that the deeper tissues were rendered less suitable for cancer inoculation after irradiation. In the cases in which the grafts took, the tendency was for the growth to go in towards the abdominal cavity. Control experiments, in which the subcutaneous graft was implanted after irradiation, showed that an erythema dose given to the intact skin does not increase the resistance of the subcutaneous tissue. A further experiment showed that irradiation of a localized area of subcutaneous tissue does not raise the general resistance to cancer implantation. Histological examination of the healing wounds showed practically no difference between control and irradiated mice up to the 5th day, but on the 7th and 9th days there was marked lymphocyte infiltration in the loose connective tissue in the irradiated animals which was still evident at the end of 14 days. P. L.-B.

Contremoulins, G. A propos de la protection des tiers contre les rayons X. [**On the protection of third parties against X-rays.**] *Compt. rend. Acad. d. sc.*, 1921, **172**, 1097. (*Arch. d'électric. méd.*, 1921, **29**, 314.)

The paper completes the one published by the author in *Comptes rendus*, 1921, **172**, 1030. Plates were exposed to X-rays behind a wall, human bones, metallic objects, and various other objects at long distances from the Coolidge tube, from 15 metres up to 80 metres. In all cases were images found on the plates, mostly very clear. From the experiments it appears that the range of the rays from a Coolidge tube is considerable: that the radiations keep the property of being diminished by the bodies they traverse in comparable proportions whatever the distance. The beam preserves for a large part its initial heterogeneity, since the images formed by the same bodies are comparable at 2, 40, and 80 metres. Under these conditions, one cannot deny, *a priori*, their biological action at a distance. This probably decreases with the intensity of the rays—that is, proportionally to the inverse square of the distance. S. E. L.-B.

Cramer, W., Drew, A. H., and Mottram, J. C. On blood-platelets; their behaviour in 'vitamin A' deficiency and after 'radiation', and their relation to bacterial infections. *Proc. Roy. Soc.*, 1922, **93** B, 449.

The authors have examined the effect of feeding rats on a diet deficient in vitamin A, and also of exposure of rats to the action of gamma rays. Their investigations were concerned chiefly with the blood changes occurring under these conditions, and in particular the behaviour of the blood-platelets.

Rats fed on a diet free from fat-soluble A vitamin after exhibiting the usual deficiency symptoms, sooner or later developed infective conditions, the eyes being frequently affected. The authors found a progressive diminution in the numbers of blood-platelets in rats fed on a vitamin A free diet—such diminution corresponding to the decline in the general condition of the animal. They also found that the infective conditions (xerophthalmia, &c.) did not develop until the number of platelets had fallen below a definite level.

Rats, when exposed to gamma rays, were found in preliminary experiments to exhibit a lymphopenia within a few hours—a polymorpholeucopenia in seven days, and an anaemia in thirteen days. Post-mortem findings proved the existence of a generalized infection with micro-organisms, accompanied by broncho-pneumonia or enteritis. When the animals were exposed to the gamma rays for shorter periods, more time elapsed before the appearance of the anaemia. The anaemia was in all cases followed by death. This led the authors to the view that the anaemia was a secondary effect, due to the invasion of the blood-stream by organisms and not directly due to the radiation. After exposing rats to gamma radiation of insufficient duration to affect the red cell or haemoglobin content, the blood-platelets showed a rapid diminution in their numbers, followed by a rapid recovery. With a more prolonged exposure no recovery to the normal platelet content took place and the animals died from some intercurrent infection.

The conclusions drawn by the authors are that, if by exposure to radium or the withholding of the fat-soluble vitamin, the number of platelets is reduced below a certain critical level, the resistance of the animal is considerably diminished, and infective conditions and anaemia may follow. The blood-platelets thus fulfil an important function in the mechanism of resistance to bacterial infection. S. R.

Radiodiagnosis

Amberson, J. B. Roentgenographic pleural annular shadows in pulmonary tuberculosis. An investigation of their clinical significance and a hypothetical explanation of the mechanism of their formation. *Am. Rev. Tuberc.*, 1921, **5**, 723–50.

At the Loomis Sanatorium Amberson has studied 50 annular shadows occurring in 36 cases of pulmonary tuberculosis. He notes that the identification of these shadows with cavities in the lungs is now generally regarded as erroneous, the present view being that they are the result of some inflammatory or mechanical change in the pleurae. Further than this authorities are not unanimous. Sampson, Heise, and Brown regard them as signs of rupture of the lung, the resulting pneumothorax, with or without fluid, being only partial on account of pleural adhesions. With this interpretation Amberson disagrees. He suggests that these shadows are the roentgenographic counterparts of simple chronic or subacute localized pleurisies, with or without localized retraction and separation of the pleural surfaces. In 14 cases there were positive or doubtful physical signs of a cavity in the lung, but in 5 of these it was the lung opposite to that showing an annular shadow which contained the cavity. 20 of the 50 shadows increased in size under observation, while 16 decreased and 12 entirely disappeared; the ring never shrank in such a way as to lose its annular character. Whenever an annular shadow developed, there were symptoms of active pulmonary tuberculosis and, conversely, this shadow never appeared when there were definite clinical or roentgenographic signs of retrogressive disease. In 19 of the 20 cases in which the shadows grew larger, the disease was active and progressive. In 27 of the 28 cases in which the shadows decreased or disappeared, the pulmonary disease was definitely retrogressive; in the remaining case it was stationary. Thus, whatever their mechanism, these shadows are of considerable prognostic importance. C. L.

Van Zwaluwenburg, J. G., and **Grabfield, G. P. The tonsillar route of infection in pulmonary tuberculosis.** *Am. Rev. Tuberc.*, 1921, **5**, 57–65.

In a report from the Department of Roentgenology of the University Hospital, Ann Arbor, Michigan, Zwaluwenburg and Grabfield correlate tuberculous infection of the tonsils with a shadow seen at the apex of the lung, commonly interpreted as a sign of localized thickening of the pleura, and known to roentgenologists as a 'pleural cap'. This shadow forms a clear line usually seen along the inner surface of the second rib, and separated from its shadow by a clear space about 3 to 4 mm. wide. It may also be seen beneath the first rib, and it sometimes extends downwards into the axilla or becomes continuous with the shadow of the thickened pleura as seen after a pleural effusion. In width it varies from a very fine line to a 3 to 4 mm. wide band. Its density varies; sometimes it is barely perceptible, sometimes it stands out with striking distinctness. Its differentiation from the linear shadows of the rib margins, and the shadows of the overlying soft tissues of the neck requires great care and good plates in stereoscopic pairs. In support of the hypothesis that this cap is of tuberculous origin, the result of downward extension of infection from the cervical lymphatics, the following evidence is adduced: In 16 cases with tuberculous lesions of the tonsils, this pleural cap was demonstrable with but one exception. Of 27 patients whose excised tonsils were found to be free from tuberculosis, only 3 showed this cap, and none of these 3 showed more than a relatively fine line without demonstrable evidence of tuberculosis in the underlying lung. To ascertain the frequency of the pleural cap in other conditions, the chest radiograms made in the laboratory over a typical three months' period were reviewed. In 30 out of 318 such records, apical pleuritis was the sole finding suggestive of tuberculosis. In the presence of cervical gland tuberculosis, apical pleuritis was demonstrable in 59 per cent., and it was probably present in other cases in which the apical shadow was obscured by that of pulmonary tuberculosis. The authors consider that the pleura offers a considerable barrier to the further progress of this hypothetical descending infection, and that the disease is frequently arrested at this point. They add that their hypothesis as to the route of infection lying through the tonsil, cervical lymphatics, apical pleura, and the lung, in the order named, may provide a satisfactory explanation for the frequency of apical lesions, the predominance of right-sided lesions, the pathogenesis of tuberculous pleurisy with effusion, and other obscure features of this infection. C. L.

Duhem, P. Signes radiologiques de l'adénopathie trachéo-bronchique. [**Radiological signs in tracheo-bronchial gland lesions.**] *Rev. méd. franç.*, 1921, January, 309. (*J. dé radiol. et d'électrol.*, 1922, **6**, 47.)

This work is of great interest and constitutes a general review of the question, since the observations contained in it include more than six hundred examinations of patients suffering from gland lesions, carried out by the author at the Hospital for Childrens' Diseases. The radiological aspect of tracheo-bronchial gland lesions differs according to whether there is found one of the five groups studied by Duhem. *First group*: Slight lesions depicted under the screen by slightly opaque and extended shadows in the region of the hilum, sometimes on the right, sometimes on the left, often on both sides; some greyish streaks may be separate, but become invisible in a few centimetres. *Second group*: If the gland reaction becomes more clear a dense opaque shadow is seen at the level of the hilum, this enlarges the median shadow of the heart and great vessels. These shadows can be multiple and confluent. A lighter zone around some of the glands indicates periadenitis or congestion of the surrounding tissues. *Third group*: Small dark spots can be seen to be separate under the screen, varying in size from small shot to a small pea. The greatest number are at the hilum, but they are scattered irregularly throughout the bronchial arborization: they are glands which have become calcified during cicatrisation. They are often accompanied by light lines of peribronchial sclerosis. *Fourth group*: The appearance of gland lesions accompanying peribronchial sclerosis: larger, more opaque, and more confluent grey lines, with small ganglion-like projections near the hilum. This represents a very advanced cicatricial process. *The fifth group* corresponds to the mediastinal gland lesions whose appearance is very characteristic, the prognosis of which varies with the intensity of the affection. S. E. L.-B.

Barret. Les signes radiologiques essentiels de la sténose du pylore. [**The essential radiological signs in pyloric stenosis.**] *Bull. Soc. radiol. méd. de France*, 1921, November, 163. (*J. de radiol. et d'électrol.*, 1922, **6**, 144.)

It is quite insufficient to base a conclusion of pyloric stenosis on a simple slowing in evacuation, since a considerable degree of slowing, whether caused by spasm or a simple dilatation, can exist without stenosis; also, owing to good compensation, a stenosis may exist without causing any slowing. Peristalsis is the first to be affected by stenosis; strong contractions can be seen which, starting almost from the superior pole, pass round the whole curvature, giving it a multilobed appearance. A phase of fatigue succeeds this period of hyperkinesia; the wall relaxes and becomes immobile. This strain on the organ ends in dilatation, but before that appears a prepyloric dilatation will be seen which is particularly marked on the lower margin of the greater curvature.

Taking these radiological signs, the smallest slowing will be significant, and it will be sufficient to differentiate a spasm from a stenosis by evacuation also; this will be long but continued in a case of stenosis and in the case of spasm intermittent, absent during the spasm, and rapid when it ceases. S. E. L.-B.

Barret. La radioscopie de la sténose du pylore chez le nourrisson. [**Radioscopy of pyloric stenosis in sucklings.**] *Bull. et mém Soc. de Chir. de Par.* 1921, **47,** 1230. (*J. de radiol. et d'électrol.*, 1922, **6**, 143.)

The diagnosis between true stenosis and spasm should be based not only on the time of emptying, but more particularly on the method, the character of the peristalsis, and the toxicity. The radiological syndrome of stenosis is made by the following signs: (a) *Irregular peristalsis*: The action is periodical, made up of intense contractions, which are exaggerated in their force and size, and followed by a period of fatigue and inertia. The intensity of the action varies according to the degree of stenosis and length of time it has existed and on the state of the musculature. (b) *Prepyloric dilatation*: This is the first indication of the giving way of the wall which precedes the great dilatation and is only related to long-standing stenosis. It is especially clear during periods of fatigue and is characterized by a cup-shaped depression at the lowest part of the stomach. (c) *Difficulties in evacuation*: Stenosis (if it be complete) diminishes the evacuating power of the pylorus but does not suppress it. Peristaltic contractions can, if powerful and frequent, compensate for the obstruction. If they become feeble, the slowness of the emptying is accentuated; therefore in forming a conclusion with regard to the slowing, the condition of the musculature must be taken into account. If, instead of a true stenosis, one is confronted with a spasm, the symptoms are quite different. The peristaltic action is diminished, not increased; the contractions are feeble, slow, and sometimes stationary. There is no phase of fatigue nor prepyloric dilatation, the wall does not relax, it remains contracted, especially in the pyloric region. Finally, the evacuation is characteristic; as long as the spasm exists the evacuation is suppressed, when it ceases there is a complete emptying: the 'all or none' rule. Pyloro-spasm can be associated with stenosis, in which case the diagnosis is very difficult and may necessitate prolonged and repeated examinations. S. E. L.-B.

Electrotherapy

Royal Society of Medicine. Discussion on the pathological changes produced in subjects rendered unconscious by electric shock. *Proc. Roy. Soc. Med.*, 1922, **15** (Sect. Elect.-Therap.), 45.

Legge said that they wanted to know whether the instructions for the treatment of persons suffering from electric shock issued under the Factory and Workshop Act were sufficient, in view of the knowledge acquired since the work of Prévost and Batelli in 1899. In 1918 Professor Boruttau attacked the apparent-death theory of Jellinek, using the statistics from the German factory inspectors' reports, which showed that artificial respiration was unsuccessful. British statistics support this. Ram referred to the increased voltage allowed by the Board of Trade since the early days. Nearly all accidents were due to touching one conductor when standing on the ground. He had noticed that a severe shock followed by a severe fall often did not produce death, and suggested that a counter mechanical shock might be of great use. The area of contact was not important. Levy said he thought there was no doubt that the commonest cause of death was fibrillation of the ventricles; the time for this to come on varied. He said that most observers agreed that currents of 1,200 volts and over, if passed from head to foot, did not affect the heart, but did so when passed through the thorax. The effect of shocks from a condensor was not cumulative, since a single shock would cause fibrillation if passed in at the exact moment of the cessation of the refractory period. He referred to the continuance of respirations after the heart had stopped beating. He believed spontaneous recovery in man was not uncommon but could not occur later than about two minutes after the onset of fibrillation. Massage of the heart was a certain means of restoring its action, but must be carried out within five minutes. If respiration were paralysed without the heart being affected then prolonged artificial respiration was indicated: as both heart and respiration might be affected, he advised artificial respiration on the remote chance of spontaneous recovery of the heart. He also spoke of disengaging a person from a live wire with the foot and not the hand. Spilsbury said it was nearly always possible to determine the points of entry and exit of the current *post mortem*. He referred to the usual post-mortem findings and gave suggestions as to the cause of death. MacWilliam said he had found two modes of immediate death: (1) arrest of respiration from paralysis while the heart continued to beat; (2) fibrillation of the ventricles. He referred to the relative frequency of these two types of death. He also advised artificial respiration in all cases and stated that massage of the heart was also of great use, especially if accompanied by the intravenous injection of drugs, several of which he mentioned, with the dose to be employed. P. L.-B.

MEDICAL SCIENCE

ABSTRACTS & REVIEWS

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In the references the letter [B] after the title signifies that the original memoir contains a good bibliography of the subject dealt with.

REVIEWS

TUBERCULOSIS

Epidemiology. According to Marantonio, during the quinquennium 1915–19, there were 2,026 fresh cases of tuberculous infection among the 2,747 patients under treatment for tuberculosis among the fighting forces of the Italian Navy. There was a total of 1,300 discharges and 158 deaths. In each of the five years, therefore, there was an average of 549 men under treatment for tuberculosis, including 405 fresh cases, 260 discharges, and 31 deaths. The days spent in hospital averaged 15,396 each year and the average duration of each individual's stay was 28·04 days. These figures apply to an average annual force of 88,526 men, and therefore yield an annual average of 6·2 per 1,000 under treatment for tuberculosis, 2·9 per 1,000 discharges, and 0·36 per 1,000 deaths from the disease. Pulmonary cases formed two-thirds of the total, and extra-pulmonary cases one-third. Although the war period was marked by an increase in pulmonary tuberculosis in the Italian Navy, this increase was too slight to justify the conclusion that the war was directly responsible for it.

In a note on tuberculosis in the French colonies, Legendre states that between the armistice and the end of June 1921, 1,662 colonists suffering from glandular, pulmonary, or osseous tuberculosis contracted in France or the occupied territories had been repatriated, their distribution being as follows: West Africans 1,071, Madagascans 364, Indo-Chinese 212, natives of the Pacific 15. Before the war tuberculosis in French West Africa was confined to the towns. In Madagascar it was almost unknown. In Indo-China it was very common, especially in Annam. In Indo-China the losses are partly repaired by the prolific tendency of the Annamites, but this is not the case in Madagascar, the black race being much less fertile than the yellow. Legendre prophesies that before long tuberculosis will be widespread throughout French West Africa and Madagascar, the natives of which are very susceptible to the disease, especially as permanent underfeeding and alcoholism are rife in these countries.

Scott, the Government bacteriologist of Hong-Kong, discusses the prevalence and character of tuberculosis in that city, and points out that it is closely connected with social and economic conditions—overcrowding and slums, poverty, insanitation, and squalor. Examination of 300 cases, aged from 6 months or under to 60 years and over, showed that in 209 or in 69·66 per cent. the primary portal of entry was the respiratory tract, and in seven others there was considerable evidence in support of the same portal, bringing the total to 216 or 72 per cent. Only 32 cases or 10·66 per cent. were definitely determined as being of alimentary origin, and five more were probably due to the same causes, making a total of 37 or 12·33 per cent. In four other cases there was a possibility of almost simultaneous entrance by way of the respiratory and alimentary tracts.

The low incidence of tuberculosis in Dortmund is emphasized by Sander, who examined 992 children up to 14 years of age with the intracutaneous test, and found that the incidence among those aged two years was barely 5 per cent. and between five and six years barely 19 per cent., while elsewhere at this age it was 50 per cent. This figure was not reached in Dortmund until the age of 13. The low incidence of tuberculosis in Dortmund was also confirmed by post-mortem examination, which showed tuberculous lesions in only 27 per cent. as compared with 40 per cent. found by Naegeli at Zurich.

Nehring, assistant at the Institute of Hygiene of Konigsberg University, examined 150 country people living in two Masurian villages, including 121 children up to the age of 14, by injection of $\frac{1}{10}$ mgm. tuberculin. With the exception of a child suffering from pernicious anaemia, all were healthy persons. Contrary to expectation, it was found that tuberculous infection was very rife in the country and increased with advance in years, so that in adult life country people were almost as frequently infected as town dwellers. The percentage of positive results for the age period 1–10 was 59; for 11–21, 72·5; and for 22–60, 91·8.

Brüning, of Rostock, examined 350 children in his private practice with Pirquet's test and found that 91 or 26 per cent. gave a positive reaction. The number of positive reactions increased with age, as is shown by the following figures: 5 out of 79 infants or 6·3 per cent., 24 out of 105 young children or 22·9 per cent., and 79 out of 166 school children or 47·4 per cent. These results, unlike those of Schlossmann, who, using the same method, found only 5 per cent., of the children in his private practice infected, show that in an agrarian region a high proportion of the children of the well-to-do classes are infected with tuberculosis, which cannot therefore be regarded as a disease of the proletariat.

Savonen's investigations of the causes of death among persons dying between the ages of 15 and 60, in a district in Finland, in the period 1897–1916, showed that, out of 17,293 deaths, 8,186, or 47 per cent. were due to pulmonary tuberculosis. He describes a scheme for securing early detection of cases of pulmonary tuberculosis in country districts. Working in co-operation with general practitioners, he travelled from parish to parish and preliminary notices of his scheme in the local press were followed up by a popular lecture or two on tuberculosis in general and the advantages of free medical examinations in particular. Then four specially trained nurses worked through the whole parish, visiting every home, scenting out early cases, and promising free medical examinations to every suspect. These promises were confirmed by written invitations addressed to every suspect. Altogether eight parishes, with a total population of 57,009, were visited during 1920 and 1921; 7,854 suspects were written to, 5,937 accepted the offer of free medical examination, and 1,034 were found to be suffering from pulmonary tuberculosis. Thus, 1·81 per cent. of the total population proved to be tuberculous. Savonen warmly recommends this system of combing out as a means towards obtaining a reliable register of the tuberculous, and putting them in touch with general practitioners and tuberculosis dispensaries.

Aetiology. Souleyre records cases showing the possibility of a very short duration of inhalation or ingestion of tubercle bacilli to determine a lesion. Thus in seven children, aged from 13 days to 12 years, the duration of exposure to infection was 2, 13, 15, 10, 1, 1, and 4 days respectively. The circumstances in each case were suckling by a tuberculous nurse, direct contact with a tuberculous mother at the time of feeding, carrying or playing with the child, indirect contact by living in the same room, bringing in the food, conversing at short distances, and a game of chess.

The teaching that the putative consumptive of adult life can be identified in childhood receives confirmation in investigations carried out by Chadwick among school children. The results of weighing and measuring 659 school children showed 71·6 per cent. to be normal, the rest to be below normal, 13·4 per cent. being 10 per cent. or more under weight. Chest examinations showed 83 to have signs suggestive of early tuberculosis, and re-examination of these 83 two weeks later enabled Chadwick to label 48 as definitely tuberculous. The children in this group showed definite impairment of resonance, d'Espine's sign, and bronchial breathing. X-ray examinations were confirmatory of the diagnosis of tuberculosis. It is pointed out that 48 out of 659 is a little over 7 per cent., and this is approximately the percentage of the present death-rate from tuberculosis. He assumes that without exceptional care and good luck many of these 48 children will die of tuberculosis.

In 1900 Turban pointed out that the site of a primary tuberculous lesion was often identical in members of one family, and among 55 families, including 121 members, he found that in 80 per cent. this familial *locus minoris resistentiae* was demonstrable. Brehmer has suggested that in one and the same family tuberculosis is liable to break out at the same age in its different members. These two hypotheses are discussed by Edel, of Marburg, whose own observations give support to both. He has studied the records of 104 families containing 222 persons, under observation in a chest hospital between 1901 and 1921. The determination of the site of the primary lesion depended on X-ray and clinical signs, such as marked retraction in some part of the chest or signs of an old pleurisy with which the disease first manifested itself. In 70 families, i. e. in 67 per cent., he found that the different members of the same family developed the primary lesion in the same site. Adding his own figures to those of Turban, Finkbeiner, Kuthy, Strandgaard, and Mayer, Edel gets a total of 444 families, including 1,013 persons, among whom there were 317 families (71·4 per cent.) showing Turban's familial *locus minoris resistentiae.* Edel also found that of 70 families there were 24 in which the members first fell ill at one and the same age (Brehmer's hypothesis in 34 per cent.). In 16 of these 24 families there was also evidence of familial *locus minoris resistentiae.* The course of the disease was also frequently the same in different members of one family, but Edel does not venture to give a statistical estimate on this point.

Rahbek publishes a long statistical paper dealing with the weights and heights of 500 children admitted to his sanatorium between 1910 and 1917. His figures do not include either patients with advanced tuberculosis or the children who could not definitely be identified as tuberculous. He found that both on admission and discharge the average height of the children was considerably above standard height, the height of boys on discharge being 2·2 per cent. and of girls on discharge 2·6 per cent. above the standard height. He asks: Does tuberculosis promote height, or height tuberculosis? The latter explanation is the right one in his opinion, for he found that the average height of the children whose disease had lasted longest was not greater than that of the other children. He also observed that the morbidity from tuberculosis followed the same curve as the rate of growth, and that the differences in the rate of growth of boys and girls at various ages coincided remarkably closely with the differences in the tuberculosis morbidity of the two sexes from time to time. Thus, if the height of both sexes at birth is put at 50 cm., boys between 7 and 14 gain 28·5 per cent. of their total height, whereas in the same age period girls gain 33·6 per cent. And this is just the age when the morbidity from tuberculosis for girls is much higher than for boys. These sex differences in the morbidity could not be accounted for by any influence school attendance might exert. It was also found that the children whose tuberculosis became manifest during the years of most rapid growth were, on the average, taller than the rest.

Symptomatology. Barlow and Thompson find that, provided skilled clinicians and radiologists co-operate, a small **pneumothorax** can be demonstrated in nearly every case of pulmonary tuberculosis at some time or other in the course of this disease. This is not a permanent pathological condition, and it usually disappears before or during the terminal illness. It is, however, definitely associated with pulmonary tuberculosis, and in a careful study of over 1,000 cases of non-tuberculous disease, these investigators have never found a small pneumothorax in the areas where it is common in tuberculosis. The symptoms of onset are often so slight that the patient does not notice them: in other cases they are similar to those of a large pneumothorax. A careful study of patients, discharged from hospital with quiescent or apparently arrested tuberculosis, and readmitted with reactivation of the disease, showed that 82 per cent. had localized pneumothoraces of such situation and extent that they caused partial or complete collapse of all parts of the lung in which there was considerable tuberculous infiltration. The suggestion is made that absence of signs of moisture in the lungs of a patient, who otherwise seems to be suffering from an active tuberculous lesion, may be due to a small, undetected pneumothorax. Stress is repeatedly laid on diagnostic skill and practice for the detection of this condition; at first both the clinician and radiologist recognize only the more obvious pneumothoraces, and it is only after several months of co-operation between the two that the greater number of these pneumothoraces are detected. Probably the demonstration of this condition is of diagnostic importance, and it should prove a valuable indication for the prolongation of treatment in cases that might otherwise relapse for want of adequate treatment.

Kalb, with an experience of 12 cases of **tuberculous empyema**, 5 of which occurred in the course of treatment by artificial pneumothorax, is greatly impressed by the value of replacing the purulent effusion by a 2 per cent. solution of formaldehyde in glycerine. From 1 to 12 ounces are injected, the amount varying according to the amount of fluid withdrawn. The amount injected should never be more than half of that withdrawn. In 2 to 7 days this treatment is repeated, and 3 to 10 days later the formaldehyde-glycerine is removed. The process is continued at certain intervals till the exudate becomes sero-sanguineous; it should now be left as it is harmless and will ultimately be absorbed. Murphy, who introduced this treatment, advocated the injection of only half an ounce of the formaldehyde-glycerine. In 7 of Kalb's cases recovery was effected, and the fatal issue in most of the remaining 5 cases was determined by extraneous factors, such as heart disease.

McKinnie, of Colorado Springs, who points out that the tuberculous basis of empyema is often overlooked, maintains that open drainage in tuberculous empyema is an unsatisfactory and often disastrous procedure when end results are considered, and that mixed infections, due to the presence of other organisms besides the tubercle bacillus, can be successfully treated by aspiration and replacement by air.

Armand-Delille and Darbois draw attention to the relatively frequent occurrence, in the pulmonary tuberculosis of children and adolescents, of **spleno-pneumonia** often simulating a pleural effusion, which is usually unilateral and involves the whole lung. The consolidation may end in slow but almost complete resolution, especially under appropriate treatment, but more frequently recovery is incomplete, and localized cavities, pulmonary sclerosis with adhesions, retraction of one side of the thorax, and deviation of the mediastinum and trachea result.

Corper and Cosman have investigated 102 cases of pulmonary tuberculosis with special reference to the various manifestations of **hypertrophic osteoarthropathy** and allied conditions. They show that, provided these conditions are carefully sought after, they can be found in most cases of pulmonary tuberculosis. The most common sites of the osseous manifestations are the distal and proximal phalanges of the hands and feet, the long bones of the arms and legs, and the bony processes of the mouth. The most common sites of the soft tissue manifestations are the tips of the fingers and toes; possibly to a certain extent the nose and malar processes. Hyperconvex finger- and toe-nails were found in 75 to 95 per cent., but there were no sex differences, and the incidence of this condition appears to be independent of the activity of the disease. But hypertrophy of the soft tissues of the hands and feet is more frequent (65 to 80 per cent.) in active than in inactive (about 45 per cent.) cases. Osseous changes are also more common in active than in inactive cases. The same difference can be observed in changes in the bony processes of the jaws. A tumour-like hypertrophy of the hard palate is demonstrable in 45 per cent. of active cases and 25 per cent. of inactive cases. It seems to be immaterial to the incidence of hypertrophic osteoarthropathy whether the pulmonary tuberculosis has been of short (1 year) or long duration (over 3 years).

Dental caries and tuberculosis. Fargin-Fayolle, Professor at the French School of Stomatology, reports the results of an investigation undertaken by his pupil Martin on the incidence of dental caries among the tuberculous. Persons in average health among the Parisian working class population showed dental caries in 20 per cent.; in subjects in the same environment suffering from various non-tuberculous medical disorders the incidence was 28 per cent., while in the tuberculous it was 33 per cent. The number of cases of dental caries in the tuberculous was thus 50 per cent. higher than in persons of average health, and more than 15 per cent. higher than in persons suffering from various non-tuberculous disorders. The writer maintains that the condition of the teeth may frequently be a guide to incipient tuberculosis, while in the tuberculous patient the presence of dental caries is an important prognostic, owing to the information which it gives as to the calcification of the patient.

Pulmonary tuberculosis and intestinal stasis. Davies's thesis, which he illustrates with numerous temperature charts and other records, is that intestinal stasis favours coliform and streptococcal infections which are largely responsible for the periodic bouts of fever from which many subjects of pulmonary tuberculosis suffer. He takes the presence of amino-acid derivatives in the urine as an index to intestinal stasis, and he has noticed that castor oil and calomel and, in certain cases, kaolin often have a remarkable effect in reducing the temperature and the quantity of the amino-acid derivatives in the urine. He has found acetone in the urine far more frequently than he expected, and these cases have been given great relief by the exhibition of large doses of sodium bicarbonate and potassium citrate. Short attacks of fever, accompanied by shivering, nausea, coryza, and increased bronchitis, were always accompanied by an increase in the amino-acid derivatives in the urine; and by giving castor oil or calomel, followed by large doses of kaolin and oil of peppermint Davies sometimes succeeded in cutting short such an attack at the onset. One patient, whose progress was constantly being interfered with by frequent recurrences of these attacks, had been free from them for over a year since he began to dose himself with castor oil at the onset of an attack. This paper is largely a plea for taking the urine as a guide to treatment of fever in pulmonary tuberculosis; if a rise of temperature is unaccompanied by any change in the urine, the tubercle bacillus is probably to blame, but if the fever and other symptoms are due to intestinal stasis, the urine shows an increase in sulpho-ethers, and the temperature returns to its old level after free purgation. The suggestion is made that the organisms in the intestinal tract are in close rapport with those causing secondary infection in the lungs, and that stimulation of the one group may affect the other. In this connexion it should be noted that the onset of intestinal symptoms is frequently associated with an increase of bronchitis in bronchitic persons.

Smoking in pulmonary tuberculosis. Duncan, of El Paso, Texas, states that his attention was called to the possibility of the untoward effects of smoking in pulmonary tuberculosis by a patient who found that cigarette smoking always caused his temperature to rise. Examination showed that the afternoon temperature after smoking was 99·3 or 99·5 and that the pulse rose from 72 or 76 to 90 or 100. If the patient abstained from smoking, the pulse continued to be 70 to 80, and no rise of temperature occurred. Duncan has since made similar observations on other patients. He attributes the phenomenon to the fact that tobacco raises the pulse-rate and to a certain extent the blood-pressure. As the result of this circulatory stimulation, there occurs an increase in the movements of the blood which is shared by the pulmonary circulation. The effect of smoking is thus analogous to that of exercise in favouring the access of toxins to the circulation. It does not, however, occur in every patient, and a decision can only be made by observation of the effect of tobacco on the particular individual.

Prenatal tuberculosis. Whitman and Greene, of Boulder, Colorado, report a case of disseminated miliary tuberculosis in a stillborn foetus in the ninth month of gestation, whose mother had an area of dullness with râles at the right apex. No animal inoculation tests were done, but the diagnosis of tuberculosis in the foetus was firmly established by the character of the histological changes and the presence of tubercle bacilli in the urine. The writers have collected 113 authentic and 519 more or less doubtful cases of prenatal tuberculosis, as well as a few others not contained in the bibliographies of Warthin and Cowie, Sitzenfrey, Péhu and Chalier, Lanz, Weber and Chomé, so that prenatal tuberculosis can no longer be regarded as a mere laboratory curiosity, but has become an urgent problem for the sanitarian.

Conjugal tuberculosis. Barnes has investigated 5,608 consecutive sanatorium cases and found that, of 2,262 married persons, 50 had consorts suffering from pulmonary tuberculosis. Probably the frequency of clinically demonstrable tuberculosis in the general population is just as high. Turning to the causes of death among the consorts of his widowed sanatorium patients, Barnes finds that 93 out of 229 widowed patients, i. e. 40 per cent., had lost their consorts by death from tuberculosis. Of over 3,400 deaths among married people under 70, only 12 per cent. were due to tuberculosis. In other words, the tuberculosis mortality among the consorts of sanatorium patients was more than three times as great as among married persons in the general community. Barnes concludes that it is unwise to assume that infection in childhood confers permanent immunity to tuberculosis.

Menstruation and tuberculosis. To ascertain whether the onset of menstruation—menarche—is earlier in women who subsequently develop tuberculosis than in women who remain healthy, Scherer has compared the age at menarche of 10,216 of his patients suffering from tuberculosis with the age at menarche of healthy women in Munich, Petrograd, Berlin, and Königsberg. The figures for these four towns were obtained from the works of Schlichting, Marcuse, Westhoff, and Rodsewitsch. The age at menarche in these four towns was, on the average, exactly 16 years, whereas it was 15·6 years, i.e. five months earlier, among Scherer's patients. Still more striking differences were obtained when he grouped his cases according as they were in the first, second, or third stage (Turban-Gerhardt) of pulmonary tuberculosis. Among first-stage cases the age at menarche was 16·05, among the second-stage cases it was 15 years, and among the third-stage cases it was only 14·726 years. Considering that his material consisted of more than 10,000 cases, Scherer maintains that these striking findings cannot be fortuitous, but indicate a fundamental law governing the date of the menarche in women subsequently developing manifest tuberculosis. By re-grouping his cases according as he considered the prognosis good, bad, or indifferent, he found that of the 5,966 patients with a favourable prognosis, only 176, or 2·95 per cent. had begun to menstruate before the completion of the fourteenth year ; whereas of the 2,699 patients with a doubtful prognosis, 848, or 31·4 per cent. had begun to menstruate before this age, and of the 1,551 patients with an unfavourable prognosis, as many as 991, or 63·9 per cent. had done so. On the other hand, the prognosis was almost invariably favourable in the 1,144 cases in which the menarche occurred after the completion of the eighteenth year. Even in the few cases in which the distribution of the disease was extensive, it almost invariably showed a chronic and benign character. Discussing the explanations for these findings, Scherer dismisses as improbable the hypothesis that early sex development predisposes to serious tuberculosis later in life, and he inclines to the view that an early menarche is indicative of an already contracted and serious tuberculous infection, the weakened organism coming to maturity earlier than usual for the same reason that, under certain conditions, weakly plants and animals mature early. The lesson of his investigations is that the girl whose menarche is abnormally early requires more care and medical supervision than others.

Tuberculosis and pregnancy. Sergent remarks that there is considerable difference of opinion as to the effect of pregnancy upon tuberculosis. While of recent years this influence has generally been regarded as unfavourable, the degree of pessimism varies, a much gloomier view being held by physicians than by obstetricians. This difference of opinion is due to the obstetricians' observations being mainly confined to the period of pregnancy and the puerperium, while physicians, especially experts in tuberculosis, chiefly see the patients a considerable time after confinement. Now it is mainly, but not invariably, some time after confinement that symptoms of fatal tuberculosis develop. Demineralization, and especially decalcification, is a well-established fact during pregnancy, is even more pronounced after confinement, and is aggravated by suprarenal insufficiency which may occur in pregnancy. Sergent is in favour of interruption of pregnancy as soon as signs of active tuberculosis develop. In three cases in which he recommended this procedure the results were most satisfactory. Good results are also reported from interruption of pregnancy by Zweifel, who states that from 1907–15 pregnancy was interrupted on account of tuberculosis in 32 cases at the Munich University Women's Clinic. 18 of these women, who had been kept under observation for at least three years, showed a considerable improvement in their condition.

Among 164 cases of tuberculosis observed by Bernard during the first six months of 1921, there were 31, or 18 per cent., who were pregnant or had been recently delivered. The injurious effect of pregnancy was more frequently seen in primiparae, 21 of the cases being primiparae and only 10 multiparae. On the other hand, there were 34 cases among the 164 patients in whom pregnancy and delivery did not appear to exercise any effect on the course of the tuberculosis. Bernard points out that an injurious effect is chiefly to be expected in the case of active caseous tuberculosis and is much less likely in localized fibroid tuberculosis (vide also *Medical Science*, 1920, **1**, 372; 1920, **2**, 235–6; 1921, **3**, 497).

Tuberculosis of the heart. According to Maresch, although tuberculous pericarditis and small nodules in the myocardium and endocardium are frequent in general miliary tuberculosis, extensive tuberculosis of the heart-wall is a rare manifestation of cardiac tuberculosis, especially in older individuals.

Stephani collected 36 cases of conglomerate tubercles of the myocardium published in the course of 93 years, and of these more than a quarter of the cases were in children under 10, and almost half in persons under 20. Adults, therefore, are much less liable than children to this rare affection. Maresch records two fatal cases in adults, aged 58 and 33 respectively, which were the only examples of this condition among 16,000 autopsies, in which, it is true, there were hardly any children. In the first case the myocardium of the right auricle was occupied by a caseous nodule the size of a hen's egg, and in the second case there was a diffuse infiltration of the left ventricle with slight invasion of the right ventricle. The clinical symptoms in such cases correspond with those of myomalacia and other myocardial changes. Occasionally, solitary nodules may be identified by their causing disturbance of conductivity.

Weiss, of Philadelphia, who records two cases, states that Norris, in a study of 7,219 autopsies, found 1,780 tuberculosis cases, and among these 82 examples of tuberculous pericarditis, in five of which the heart-muscle was involved. In Weiss's cases, which occurred in men both aged 25, the symptoms and signs were vague; the necropsy showed an immense fibro-caseous tuberculous involvement of the thoracic lymph nodes with extension to the pericardium, and in one case to the heart-muscle, causing tremendous enlargement of the organ. The literature shows that tuberculous disease of the heart is almost always secondary to involvement of the mediastinal lymph glands.

According to Benvenuti, of Como, who reports a case of tuberculosis of the myocardium in a man aged 24, the first example of this condition was recorded by Laennec in 1826, and the next by Townsend in 1832. Numerous cases were subsequently described, so that Raviart, in 1906, was able to collect 185 cases. The autopsy in Benvenuti's case showed tuberculosis of the left lung, and a large obsolete tubercle in the left ventricle. In most cases, as in that described by Benvenuti, tuberculosis of the myocardium develops in an insidious and latent manner, so that Dieulafoy regarded it as merely an autopsy finding without any clinical history. Benvenuti, however, suggests that the functional cardiac disturbance that predominates in the last stage of the disease, as it did in his own case, and is generally attributed to toxaemia, is sometimes due to secondary localization of tuberculosis in the myocardium.

Korybut-Daskiewicz, of Warsaw, records a unique case of tuberculosis of the heart in a male infant, aged 1 year and 8 months, whose mother had died of pulmonary tuberculosis. In addition to an infarct in the left lung, diffuse bronchitis and peribronchitis and a small cavity at the right apex, the autopsy on the infant showed a ruptured aneurysm at the apex of the heart, which was the cause of sudden death. There was also tuberculous endo-, peri-, and myo-carditis, and increase in size of the mesenteric glands, some of which were caseous. There had been no signs of severe cardiac disease during life.

Diagnosis. According to Brown, the five cardinal diagnostic points in pulmonary tuberculosis are (1) tubercle bacilli, (2) moderately coarse râles, (3) a parenchymatous Röntgen-ray lesion above the second rib and third vertebral spine, (4) haemoptysis of one drachm or more, (5) pleurisy with effusion. At least one or more of these points must be present before a diagnosis of pulmonary tuberculosis can be made. If all five cardinal diagnostic points are absent, a negative diagnosis as regards pulmonary tuberculosis may be made, but in 1 or 2 per cent. there may be an error.

At the Children's Hospital attached to the Hamburg University, Kleinschmidt has carried out comparative cutaneous tests with tuberculins made from bovine and human tubercle bacilli and from a mixture of the two. He comes to the conclusion that bovine tuberculin provides no reliable evidence as to the type of infection from which the patient is suffering. Tuberculin of the human type is, on the whole, more effective for the skin test than either pure bovine tuberculin or a mixture of the two.

According to Rosenblatt, the great majority of basal lesions are not tuberculous. Among 1,000 consecutive cases admitted to the Bedford Sanatorium, New York, he found that there were only three with definite primary lower lobe tuberculosis. Particular care, therefore, should be exercised before diagnosing tuberculosis in a patient with a lower lobe lesion. X-ray evidence is of paramount importance when no tubercle bacilli can be found in the sputum. In non-specific lung infection and bronchiectasis—the two conditions most likely to be mistaken for tuberculosis—the skiagram is usually clear, even when extensive physical signs are found, while tuberculous lesions of equal extent never fail to give evidence of their existence.

Prognosis. Würtzen has published a monograph under the auspices of the Danish Life Insurance Companies' Committee for Sub-standard Lives on the duration of fatal pulmonary tuberculosis. After reviewing earlier investigations, he passes on to his own, which cover a period of 13¾ years (April 1906 to the end of 1919), and which deal with 1,032 men, 780 women, and 87 children who died in this period after admission to a tuberculosis hospital in Copenhagen. These persons belonged to the working classes, and the mean duration of the disease was calculated by dividing the months of illness, from the first appearance of symptoms to death, by the number of patients. The result was 35·9 months. The influence of diabetes and syphilis was studied in separate classes, and they were shown to reduce the expectation of life considerably. For 10 cases of diabetes plus tuberculosis the mean duration of life was 7½ months, and for 47 cases of syphilis plus tuberculosis it was 27½ months. To gauge the effect of sanatorium treatment on the duration of life, the 339 patients given this treatment were grouped together and found to show a mean duration of 56·1 months, as compared with 35·9 months for both sanatorium and non-sanatorium cases. This difference in favour of the sanatorium cases was all the more striking as they included several cases of acute disease which had been discharged early from a sanatorium because they could not benefit from this treatment. When he classified his material in age groups Würtzen found that the duration of fatal tuberculosis is not shorter between 15 and 30 than after this age, and he suggests that the common view that pulmonary tuberculosis is most dangerous up to the age of 30 depends on a confusion of the *incidence* of the disease with its *malignancy* at different ages. But below the age of 15, and again in old age, the disease ran a comparatively rapid course.

Burnand, director of the Leysin Popular Sanatorium, addressed a questionnaire to 1,340 patients who had been discharged between 1912 and 1917, and received replies from 644. Of the total 438, who had been discharged as cured or improved, 277, or 63·24 per cent., were fit for work, only 11 were ill, and 161 had died. Burnand concludes that the selection of patients for the sanatorium should be increasingly strict and made as early as possible, as it is only on these conditions that permanently good results can be obtained. He considers that a popular sanatorium should treat only mild cases, and should discharge without delay severe cases which are not improved by one or two months' treatment. As a general principle the treatment should be long, and, if necessary, repeated.

Block has investigated the after-histories of 738 patients suffering from chronic pulmonary tuberculosis, distinguishing between those who had, or had not, suffered from pleurisy with effusion. He publishes an elaborate system of classification and shows that the prognosis is far worse for patients who have suffered from pleurisy.

The influence of pleural effusions on the subsequent course of pulmonary tuberculosis is the subject of a statistical survey by Országh, of Buda Pesth. During the past six years, 22, or 1·2 per cent., of his patients suffered from a pleural effusion. Adding several other cases, not personally observed, he gets a total of 54, of whom 23, or 43·6 per cent., showed improvement after the effusion. He finds that the mortality for the cases complicated by pleural effusions was 55·8 per cent. as compared with only 45 per cent. among the cases not thus complicated. His conclusion that, on the whole, a pleural effusion is injurious sooner or later, is confirmed by cutaneous tuberculin tests made in 16 cases during an attack of pleurisy with effusion. In as many as 14 of these cases the reaction was negative, showing that the patients' resistance was lowered. On the other hand, 5 out of 6 patients developing a pleural effusion in the course of pneumothorax treatment gave a well-defined positive reaction. These differences may be correlated with the observation that a pleural effusion in the course of pneumothorax treatment often runs a symptom-free course, whereas the spontaneous pleural effusion is commonly associated with profound constitutional disturbances.

At Romberg's hospital in Munich, Kleeman has studied the behaviour of leucocytes in pulmonary tuberculosis and has come to the conclusion that the total number of leucocytes is of no diagnostic or prognostic value. She found lymphocytosis in the mildest cases on the way to recovery, and regards it as indicating a favourable prognosis. In the absence of complications in severe cases of pulmonary tuberculosis, neutrophilia is of bad prognosis, but it may occur in slight cases complicated by haemoptysis or secondary infection. Eosinophilia was observed as occurring spontaneously or after the administration of tuberculin in cases running a favourable course. As recovery proceeded, the number of eosinophils returned to normal; their absence is a bad prognostic sign. Changes occurring spontaneously or as a result of tuberculin injections may sometimes be reflected in the blood count before any other symptom.

In a paper on the presence, absence, and location of râles in the prognosis of pulmonary tuberculosis, based on the study of 1,000 consecutive admissions to the Trudeau Sanatorium from 1907 to 1913, Trudeau comes to the following conclusions: (1) Cases in which no râles were found either on admission or on discharge showed the highest percentage of cures. (2) Patients admitted with râles, but who lost them during their stay in the sanatorium, formed nearly as favourable a group as those who had never had any râles. (3) In patients who were admitted without râles, but developed them during treatment, the prognosis was much graver than in either of the other two groups. (4) In spite of greater frequency of tubercle bacilli in right upper lobe lesions as contrasted with those of the left upper lobe, the prognosis is considerably more favourable in the former class. (5) Basal râles should not be diagnosed as non-tuberculous too lightly, for in nearly 50 per cent. of this series tubercle bacilli were found in the sputum, and nearly 40 per cent. of these developed apical râles during their stay in the sanatorium. (6) The prognosis among cases in which the râles were limited to one or both bases was not more grave than in patients with râles over one or both lobes.

In answer to the question : Does persistence of râles indicate persistence of active pulmonary tuberculosis ? Löwenhjelm records in detail three cases of pulmonary tuberculosis of long standing. In every case râles continued to be heard almost up to the time of death, which in no case was directly due to the pulmonary tuberculosis. The necropsies showed no recent tubercles or signs of activity in old tuberculous areas. But it was noticed that the râles heard corresponded to those parts of the lungs where healed tuberculous foci were found *post mortem*. As pleural adhesions are often situated over such foci, it may be that sounds interpreted by the physician as râles were really due to creaking in and about pleural adhesions; like many other authorities, Löwenhjelm confesses to being unable invariably to distinguish between pleural and pulmonary adventitious sounds. The upshot of his investigations is the verdict that it is unwise to rely on adventitious sounds in the lungs as proof positive of active pulmonary tuberculosis when this evidence is unsupported by other signs of active disease.

Treatment. The value of calcium therapy in tuberculosis has recently been emphasized by numerous writers, especially Tweddell in the United States and Coutière in France, who draw attention to the immunity to tuberculosis of workers in lime and plaster of Paris. Coutière has found that inhalation of calcium powders 10 to 12 times a day for 5 minutes or more at a time is followed by disappearance of the physical signs and by a gain in weight and strength. Tweddell has found intravenous injection of calcium in colloidal form extremely efficient in the treatment of incipient tuberculosis. He has always used it in conjunction with inhalations of sulphur dioxide (vide *Medical Science*, 1921, **3**, 498), except in cases of haemorrhage, where he used calcium alone.

In addition to a brief survey of the most recent literature of calcium therapy in tuberculosis, Maendl, who has treated about 250 cases of pulmonary tuberculosis with about 4,000 intravenous injections of calcium salts, discusses the merits and shortcomings of this line of treatment. He is not much impressed by it, and he admits that he has never succeeded in bringing down a very high temperature by it. On the other hand, a great number of cases with a subfebrile temperature, which is so difficult to influence by ordinary means, responded to this calcium treatment by a fall of the temperature to normal. Other symptoms referred to are cough, expectoration, night-sweats, and dyspnoea, on all of which this treatment exercised a salutary effect in many cases. The dosage recommended for the treatment of haemoptysis is 5 c.cm. of a 10 per cent. calcium chloride solution, repeated at 8-hour intervals for as long as necessary. Apart from haemoptysis, the drug is given every or every other day, and pauses of one or two weeks are allowed between courses of about 20 injections. By the addition of 0·25 gm. of antipyrin to a 10 per cent. solution of calcium lactate, various discomforts associated with the injection of the calcium salt alone can be avoided. When some of the salt is deposited in the tissues outside a vein, necrosis is apt to follow unless the tissues are massaged so as to hasten the absorption of the calcium.

Ringer and Minor have given intravenous injections of calcium chloride (5 to 10 c.cm. of a 5 per cent. solution) in 30 cases of tuberculous diarrhoea, and though they have to register failures in as many as 13 cases, they have come to the conclusion that this procedure is often remarkably beneficial, relieving pain and discomfort, and greatly reducing the frequency of the motions. In cases given numerous injections they appear to lose some of their efficacy and have to be repeated at shorter intervals. Thus, in one case the effects of an injection lasted at first for about a month. Twenty months later it was necessary to give an injection every 10 days, and to increase the dose from 5 to 8 c.cm. to keep the action of the bowels more or less normal. The authors confess that this treatment is based on empiricism, but of its good effects they have no doubts; they refer to the work of several Swedish physicians who have found that the intravenous injection of calcium chloride diminishes diarrhoea and relieves pain.

Intravenous injections of calcium chloride have also been used with success for vomiting and diarrhoea in pulmonary tuberculosis by Pellé of Rennes, Merklen and Dubois-Roquebert, and Efrémidès. The last writer, whose thesis is based on 74 cases treated in Rist's service at the Hôpital

Laennec, in Paris, states that 2 c.cm. of a 50 per cent. solution was used, the injection being repeated once or twice on the following days if necessary.

Müller, with an experience of 572 cases, observed over a period of several years, believes he has found in guaiacol-iodoform, given by intravenous injection, a valuable remedy for pulmonary tuberculosis. This combination was introduced in 1880 by Mosetig, the proportions being 4 parts of guaiacol to 1 part of iodoform. Müller first gave this mixture by the rectum, but found it reacted unsatisfactorily. For intravenous injection he uses 3 solutions, the first containing equal parts of olive oil and of guaiacol-iodoform, the second containing only 20 parts of olive oil to 100 parts of guaiacol-iodoform. The third solution contains pure guaiacol-iodoform. He gives 2 intravenous injections every week, and for the first 4 weeks only the first solution is given, the dose at each injection being gradually increased from 0·25 to 1 c.cm. The second solution is then given twice a week for the next 4 weeks, the dosage again being 0·25 to 1 c.cm. The undiluted guaiacol-iodoform is then given twice a week in doses of 0·25 to 1 c.cm. Müller chose chiefly second and third stage, sputum-positive cases with signs of active disease for this treatment, the results of which he discusses in rather vague, though highly laudatory terms. He refers to disappearance of tubercle bacilli and the germs of mixed infection from the sputum, to a return of the temperature to normal, and to other signs of recovery in 'many hundred cases'. A complete course of treatment consists of about 40 injections. He has seen no signs of iodoform poisoning, but he refers to 12 cases in which a rapid fall of the temperature to normal was followed by transitory lassitude, a sense of anxiety, and brief cardiac insufficiency.

Rickmann has treated 52 cases of tuberculosis with krysolgan, and in about 40 per cent. he has observed improvement. This was most marked in the case of tuberculosis of the larynx; the effect of the drug on tuberculosis of the lungs was disappointing. The chief feature of Rickmann's paper is his tale of ill effects, such as lassitude, giddiness, and hyperpyrexia. Patients, whose urine had previously contained no albumin, developed albuminuria, and one patient, who was given 0·2 gm. at the third injection, developed acute haemorrhagic nephritis. More or less severe gastro-intestinal disturbances were not uncommon, and two patients reacted regularly to each injection of 0·05 gm. by violent diarrhoea and a rise of temperature to 39°; not till a week or two later did this violent reaction subside. Another patient developed a severe rash accompanied by alarming general disturbances after the tenth injection of 0·2 gm. After all these misfortunes Rickmann is inclined to shelve krysolgan, and the only incentive he finds to continue its administration is its apparently specific effect on laryngeal disease.

Schellenberg's experience of krysolgan covers the period 1917–20, and concerns 79 patients. The intravenous injections were well tolerated in most cases, but in several complications occurred, such as vomiting, giddiness, pain in the back and head, profuse perspiration, albuminuria (one case only), palpitation of the heart, and other symptoms. Only in three cases did the patients declare they felt better for the treatment, and Schellenberg confesses to being thoroughly disillusioned, his results being so much less promising than those of earlier writers. Possibly, however, tuberculosis limited to the larynx, bony system, or skin may benefit, and in four cases of tuberculosis of the larynx definite improvement certainly did follow this treatment.

Armand-Delille, Hillemand, and Lestocquoy treated 32 cases of pulmonary tuberculosis by subcutaneous injections of oxygen. In almost all there ensued improvement of the general condition with increase of appetite and a sense of well-being, though the writers admit that similar results are observed in tuberculosis patients whenever a new treatment is adopted. On the other hand, the following changes occurred in the blood, indicating that the treatment was not devoid of physiological action: (1) a fairly marked diminution of leucocytosis, (2) increase of the polymorphonuclears and lymphocytes at the expense of the mononuclears, (3) transient increase in the number of the red cells after the first injection. The treatment is absolutely harmless, provided the injections are not given too frequently to thin subjects, and may be employed advantageously in conjunction with other methods.

Pissavy states that the value of the treatment of haemoptysis by extract of the posterior lobe of the hypophysis introduced by Wiggers in 1911 was confirmed by Rist in 1913 and subsequently by L. Bernard and Émile-Weil. At the present time intravenous injection of the drug constitutes the sole treatment of severe haemoptysis in Pissavy's tuberculosis service at the Cochin Hospital, in Paris. 1 c.cm. of the extract is mixed with 10 c.cm. of saline solution and injected slowly into an arm vein. In half the cases the haemostasis does not become complete until after a series of injections, so that Pissavy is in the habit of giving three consecutive injections at intervals of twenty-four hours, and in the great majority of cases he thus succeeds in preventing relapses. He points out that the haemostatic action of pituitary extract is due to its increasing the coagulability of the blood, as has been shown by Weil and Boye, Lidon and Porak.

Five cases illustrating the successful employment of subcutaneous injections of retropituitrin are reported by Trancoff.

Saggis records five cases of haemoptysis successfully treated by intramuscular injection of emetine after almost all the usual remedies had failed. The doses consisted of 3 cgm. of emetine hydrochloride, from 1–5 injections being given. Owing to its hypotensive action the drug is contra-indicated in cases with low blood-pressure.

Minnig has given autogenons vaccines in 63 cases of pulmonary tuberculosis, and, as a rule, only one organism to a vaccine was used. He considers stock vaccines as useless, and the organism which gave the best results was the *Streptococcus haemolyticus*. In 32 cases, 15 of which were in the third stage of the disease, improvement was effected. Minnig's verdict is favourable but reserved, and he considers a persistently high temperature and certain other conditions as contra-indications.

Neuer's analysis of 91 cases of pulmonary tuberculosis selected for pneumothorax treatment since 1908, at a hospital in Schömberg, brings out several points of importance in the choice of suitable cases. As she remarks, the present standards for such choice are unsatisfactory, apparently suitable cases proving most disappointing, while cases considered barely suitable react most satisfactorily. As her figures show, the prognosis depends much less on the extent and distribution of tubercle in the body than on the character of the disease and the organism's reaction thereto. Classifying her cases according as they were, or were not, complicated by other, non-tuberculous diseases, she shows that these complications were impartially distributed among the successes and failures. Such diseases of the heart, kidneys, and other organs should not, therefore, be regarded as contra-indications to this treatment. It is generally held that the success of a pneumothorax largely depends on limitation of the disease to the collapsed lung. Neuer's results suggest that this teaching is misleading. Almost invariably tuberculous disease in the larynx, intestines, the sounder lung, and other parts of the body was stationary or became arrested when adequate collapse of the most diseased lung was effected; whereas when such collapse was prevented by adhesions the disease in these distant parts was progressive. But though the immediate and ultimate results of an artificial pneumothorax are, as a rule, strikingly beneficial, there is an intermediate stage—usually in the second and third months of treatment—when secondary eruptions of tubercle occur, either in the form of pleural effusions on the pneumothorax side, or as more distant foci in the sounder lung or elsewhere. These secondary eruptions are evidently determined by the treatment, for they are very rare in cases in which a pneumothorax cannot be induced on account of adhesions. In 16 such cases there were only two instances of such secondary eruptions, whereas among 26 cases in which a pneumothorax was induced, but the patient did not benefit therefrom, there were as many as 35 secondary eruptions, not including pleurisies on the pneumothorax side. Neuer develops the hypothesis that collapse of a tuberculous lung is apt temporarily to rob the body of defensive forces provoked by a focus of active disease, and she compares her pneumothorax experience with that of surgeons who, after the radical removal of tuberculous bones and joints, find tubercle rapidly developing elsewhere. As her figures show, the proportion of failures was great among cases in which the disease had lasted less than a year, while many of her greatest successes were in cases of many years' standing. Only in three cases has she seen 'malignant' phthisis benefit from this treatment.

Liebe's survey of 104 cases treated since 1915 at the Waldhof-Elgershausen Sanatorium, shows that in 31 no pneumothorax could be induced on account of pleural adhesions. In 73 a pneumothorax was induced, and of these, 7 could not be subsequently traced. In 32 cases the ultimate results were satisfactory, the pneumothorax having been re-absorbed in 16, and still being maintained in 16 cases. Liebe has given up injecting morphine before the operation on account of the disturbances it provoked. Discussing the choice of gas, she refers to a recent pronouncement by Brauer, who disputed the teaching that the risk of embolism is greater with air than with oxygen. All the same, Liebe usually gives oxygen at a first injection, when the readings of the manometer are dubious. With regard to these readings, she points out that definite oscillations may be obtained when the point of the needle is superficial to, or beyond, both layers of the pleurae, as well as when it is in the pleural cavity. Among the 31 cases in which no pneumothorax could be induced, collapse occurred in 3 cases; in 2 it was not clear whether this was due to embolism or pleural reflex; in the third the pallor, cyanosis, absence of pulse, and twitching of the face on the opposite side suggested embolism. Among the 73 cases in which a pneumothorax was induced, there were 11 cases of collapse, 3 of which were certainly due to embolism. Three others were certainly due to pleural reflex, and in 4 other cases the cause of the shock was in doubt. In the eleventh case the collapse was due to vomiting, for which the morphine was probably responsible. Apparently none of these cases terminated fatally. In 26 cases a pleural effusion occurred, but in no case did this turn to an empyema.

Miller analyses the results achieved over a period of seven years, in 50 cases of pulmonary tuberculosis, by the induction of a pneumothorax. The disease was in the second stage in 13, and in the third stage in 37 cases. One to seven years after treatment the results were: well and working, 17 (34 per cent.); living, but not working, 16 (32 per cent.); and dead, 17 (34 per cent.). Considering the type of cases selected for this treatment, Miller considers his results excellent, and he states that he adopts this treatment more frequently every year. Merely as a palliative measure he has found it of value, and he urges that it should not be postponed till the patient has drifted into such a condition that intrapleural adhesions prevent its adoption.

Peters has seen 26 cases of purulent effusion into the pleural cavity among 250 patients in whom he induced, or attempted to induce, an artificial pneumothorax. In all these 26 cases the effusion was subjected to a bacteriological examination; in 8 there was a mixed infection, and in the remaining 18 only the tubercle bacillus was found. In the 8 cases of mixed infection drainage was effected, but 6 soon terminated fatally. One of the remaining patients enjoyed excellent health for four years, and then the disease recurred and death followed. All the 18 cases without mixed infection recovered temporarily, and in 10 of these cases their subsequent fate was ascertained. Of these, 4 had died and the remaining 6 were doing well. Peters concludes that for these cases of simple purulent effusion, uncomplicated by mixed infection, expectant treatment should be adopted, and the fluid should be removed only when relief of pressure symptoms is indicated. The average patient with simple tuberculous pus recovers as easily and quickly as the patient with only a sero-fibrinous effusion. When the infection is mixed, drainage is indicated, but the prognosis is usually hopeless.

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THE WORK OF MAGNUS AND HIS COLLABORATORS ON THE NERVOUS REGULATION OF POSTURE, AND ITS BEARING ON SOME MODERN NEUROLOGICAL PROBLEMS

Introduction. The significance of muscle-tone as the basis of all postural reactions has been revealed to us during the past five-and-twenty years by the classic researches of Sherrington. We now know that the old definition of skeletal muscle-tone as 'that state of active tension characteristic of living muscle in connexion with the nervous system' is profoundly inadequate. The experimental preparation employed by Sherrington in his studies on the nature and significance of muscle-tone is the so-called 'decerebrate animal'. This is a mammal (rabbit, cat, dog, or monkey) in which the brain-stem has been divided in the region of the tentorium. In these circumstances the extensor groups of muscles enter almost at once into a state of heightened tone which provides an excellent medium for the analysis of the phenomenon. The muscles affected are found to be those which maintain the animal in the standing position. For this and other reasons into which we cannot now enter, Sherrington has concluded that muscle-tone is 'reflex posture' and that 'decerebrate rigidity' is 'reflex standing'. He has further demonstrated how intimately tone enters into the processes of motor co-ordination. Postural or tonic reactions provide the medium in which all co-ordinated movement takes place, and when they are abolished the grossest disorders of co-ordination result. It now seems almost certain that in cerebellar ataxy we have a characteristic and striking example of such loss of postural tone (cf. *Medical Science*, 1922, **6**, 131).

The centres essential to the maintenance of decerebrate rigidity were found by Sherrington, and later by Thiele and by Magnus, to lie exclusively in the brain-stem caudad to the plane of the anterior corpora quadrigemina. Transections cephalad to this plane are not followed by rigidity, and when rigidity is once produced by appropriate transection it is invariably abolished by transections caudad to the plane of the calamus scriptorius (Sherrington, Magnus). Neither the centres nor their afferent or efferent paths lie in the cerebellum.

We are here primarily concerned with the more recent investigations into the nervous regulation of muscle-tone, which have been carried out at Utrecht by Magnus and his co-workers during the last ten years. This work is recorded in a series of over twenty papers, and it is seldom that the literature of experimental physiology has contained a more fascinating story of ingenious experiments, of difficulties overcome, and of knowledge gained. Moreover, it is at once apparent to the reader that here we have information of the greatest importance to us as clinical neurologists in our attempts at the physiological analysis of the motor disorders arising from disease of the central nervous system. At a moment when neuropathologists are throwing themselves with such zest into the problems, pathological and physiological, presented by the so-called ‘corpus striatum syndromes’, it may not be superfluous to remind ourselves that our labours are almost certainly foredoomed to disappointment until we have acquired a sound working knowledge of the functions of the lower level nervous mechanisms situated in the brain-stem. Indeed, it is steadily becoming more apparent that very many of the functions now attributed to the corpus striatum are subserved by midbrain mechanisms, our knowledge of which we owe principally to the work now under review.

Tonic labyrinthine and neck reflexes : standing reflexes. In the course of his experiments, Sherrington (*J. Physiol.*, 1910, **40**, 112) had observed that while the tone of a given muscle depended essentially upon the integrity of its afferent nerve-supply, yet it was not wholly independent of afferent impulses from other regions. Thus, active or passive rotation of the head of the decerebrate animal upon the neck inhibited the extensor tone in the limbs of that side of the body to which the vertex was turned. That this was not due to labyrinthine stimulation was proved by the persistence of the reaction after bilateral section of the eighth nerve, and its origin was revealed when bilateral section of the posterior roots of the upper cervical spinal nerves was found to abolish the reaction. In short, the reflex arose in the afferent nerves of the neck-muscles. Still utilizing the decerebrate animal, Magnus and de Kleijn found that by varying the position of the animal's head in relation to space and in relation to the neck and trunk it was possible to produce certain constant modifications in the tonus of the neck, trunk, and limb muscles, and thus in the posture of the animal. The existence of two groups of reflexes was determined, labyrinthine and neck reflexes. In each case the reactions are tonic in the sense that they are produced, not by movement, but by the changed posture of the head, and they persist so long as the new posture is maintained, even though this be for months. The *labyrinthine reflexes* (‘tonische Labyrinthreflexe’) arise from stimulation of the otolith organs of the labyrinths when the position of these in space is changed in relation to the horizontal plane. Their effect is to reinforce the extensor tonus of the body musculature, and this influence is maximal when the animal lies on its back with the line of the mouth (‘Mundspalte’) making an angle of 45° above the horizontal. There is also a position of minimal influence, namely, with the animal standing and the line of the mouth at an angle of 45° below the horizontal. In all other positions the degree of extensor tonus is proportional to their approximation to the maximal and minimal positions of the animal. These positions have been found to be similar for all animals, from the guinea-pig to man. The labyrinths affect all four limbs identically (identical innervation). Destruction of these organs abolishes the reactions, and variations in the position of the head in space no longer modify muscle-tone, but it is still possible to achieve this result by varying the position of the head in relation to the neck and trunk ('tonische Halsreflexe'). The *neck reflexes* arise in the proprioceptive nerve endings of the cervical muscles and can be investigated free from complication after bilateral destruction of the labyrinths. It is then found that *rotation of the head* on its long axis ('Drehung' axis-snout foramen magnus), *lateral flexion* ('Wendung'), *dorsal flexion* ('Hebung oder Dorsalbeugung'), and *ventral flexion* ('Senkung oder Ventralbeugung') produce constant changes in muscle-tone and posture. Thus, rotation of the head to the right (vertex to right, snout to left) causes increased extensor tonus in the limbs of the left side (the side to which the snout points, 'Kieferbeine'), and abolition of extensor tone in the limbs of the right side ('Schädelbeine'). Lateral flexion of the head to the right causes increased extensor tonus in the right limbs and diminished or abolished extensor tonus in the left limbs. Thus combined rotation and lateral flexion to the right antagonize in their effects, but, since the former is the more effective stimulus, the rotation effect still persists, though in diminished intensity. Hence, we see that alterations in the symmetrical relationship of the head to the trunk affect the limbs of the two sides reciprocally, and not identically. Dorsal flexion of the head produces in the rabbit increased extensor tonus in all four limbs, so that the sitting animal rises on its legs, while ventral flexion has the reverse effect. In other animals, however, the fore and hind limbs are reciprocally affected, so that dorsal flexion increases fore-limb extensor tonus and abolishes that of the hind limbs, so that the animal sits up. Ventral flexion abolishes extensor tonus in the fore limbs and increases it in the hind limbs, so that the animal appears in the position of looking down on the floor ('looking under a low shelf'). An additional reaction, the *vertebra prominens reflex*, is also described. Here, pressure directed ventrally on the spine of this vertebra causes abolition of extensor tone in all the limbs and the standing animal sinks down into a sitting position. The labyrinthine reflexes can also be studied, apart from those arising in the neck muscles, by fixing the head and trunk in a plaster bandage. When both groups are in action simultaneously a great variety of postural reactions can be observed, for it is clear that they combine differently according to the initial position of the animal. Therefore they have been investigated with the animal in five positions, vertical with head above and head below, right and left lateral, and prone and supine positions. In this way, Magnus and de Kleijn have analysed what at first sight appeared to be a chaos of inconstant responses into their component elements. The task was made still more difficult by the fact that while in certain individual animals the labyrinthine reflexes predominate, in others those from the neck muscles are the more powerful.

We are now in a position to consider the results of *unilateral labyrinth destruction*, and in this respect Magnus and de Kleijn have been able to amplify the well-known work of Ewald in a remarkable manner. They have investigated animals of various species—frog, guinea-pig, cat, and dog—and although the results vary in detail, yet in broad outline they are the same. In the case of the rabbit, the immediate results are skew deviation of the eyes and nystagmus, rotation and lateral flexion of the head to the side of the lesion, some spiral rotation of the neck and trunk to the side of the lesion, and alterations in the extensor tonus of the limb muscles—diminution on the side of the lesion and increase on the crossed side. Rolling movements also are frequently seen, but are not constant. Of these symptoms some are permanent and some transient. In the latter group are nystagmus and rolling movements. Rotation of the head and neck and reciprocal alterations in limb muscle tonus and deviation of the eyes are permanent. We may take these symptoms singly. In the rabbit the deviation of the eye is a 'skew deviation'. The eye on the side of the lesion is displaced ventrally, and the crossed eye dorsally. The nystagmus has a quick component to the midline with a slow return to the affected side. In the cat and dog, where the eyes are less laterally placed in the head, the deviation is mainly lateral—to the side of the lesion—and the 'skew' is minimal or absent. If the head be passively rotated to the normal side, the deviation becomes maximal and the nystagmus ceases. The rotation of the head to the affected side is permanent and tends to increase for several weeks after the operation, and it may occur through more than a right angle. The corresponding spiral rotation of the neck and trunk varies in different animal species, being minimal in the cat and dog, maximal in guinea-pig and rabbit, and it is not so long lasting as the head rotation. The diminished extensor tonus of the homolateral limbs and the increased extensor tonus of the crossed limbs are permanent. Further analysis shows that the permanent symptoms may be divided into primary or direct, and secondary or indirect. The *direct symptoms* are the immediate result of loss of a labyrinth and unbalanced action of the intact organ; they include eye deviation and rotation of the head. The *indirect symptoms* are due to the rotation of the head, which sets up neck reflexes secondarily. These in turn cause the reciprocal tonus changes in the limbs and are mainly responsible for the spiral rotation of the trunk. Hence, we see that some of the most striking results of loss of one labyrinth are only indirectly caused, and they disappear at once when the head is passively righted. The direct effect of loss of one labyrinth is very transiently to diminish the extensor tonus in the homolateral limbs. Magnus and de Kleijn have been able to clear up the uncertainty surrounding the genesis of the rolling movements, which have been so frequently described and so variously interpreted, by the careful study of kinematographic records. They arise as running or leaping movements in an animal whose trunk is spirally rotated so that it progresses like a screw. Two leaps go to a complete rotation. The movements occur in 'attacks', which the observers attribute to irritation arising in the wound and probably involving the central stump of the eighth nerve. While, therefore, in one sense the rolling movement may be regarded as an 'irritation' symptom, yet the actual rotation is the result of unopposed action of labyrinthine and neck reflexes on one side, and as such may be regarded as a 'release' symptom. From these observations Magnus and de Kleijn conclude that each labyrinth influences the tonus of the limb muscles of both sides equally, the trunk- and eye-muscles bilaterally, but chiefly those of the opposite side, and the neck-muscles of one side only. Nowhere in their papers do they state explicitly that this neck influence is crossed, but it seems clear that this must be the case, for the rotation and lateral flexion of the head to the side of the destroyed labyrinth is found to be due to increased tonus in the cervical muscles of that side. The increase is greatest in the maximal and least in the minimal position of the animal, which were described earlier. The neck-muscles of the side on which is the intact labyrinth are atonic and show no variation in any position of the animal. In other words, the influence of the intact labyrinth is on the crossed muscles, as Ewald taught.

Postural reflexes ('Stellreflexe') in the 'thalamus' and 'midbrain'

animals. We have seen that the posture of the head ('the leading segment', Sherrington) determines the attitude of the whole body ('Körperstellung'), and in the decerebrate animal, by using the head as a handle, we can vary the body-posture at will. However, we have only to consider the capacity of the normal animal to vary the position of its head and of its trunk at need, to realize that the reflexes we have so far studied are not the sum total of the postural reflexes active in the intact animal. The decerebrate animal possesses no reflex by which the position of its head can be actively modified. The head is unalterably retracted. Hence the animal can do nothing but stand. If a reflex movement be elicited by appropriate stimulation the animal loses its balance and falls, and has no power of righting itself. Indeed it can stand only when it is carefully placed upon its feet. Further, Magnus points out that this 'reflex standing' is merely a caricature of the normal function, while the incidence of tone in the muscles is abnormal, that of the extensors being exaggerated at the expense of the antagonist flexor groups. It is clear, therefore, that we look in the higher levels of the nervous system for these postural reactions which the normal animal possesses and the so-called decerebrate animal lacks.

For this purpose Magnus has made use of the 'thalamus' and 'midbrain' preparations. In an animal—rabbit, cat, dog, or monkey—the whole of the cerebral hemispheres, including the corpora striata are removed. The thalamus, subthalamic region, and midbrain remaining intact. The 'midbrain' preparation is one in which the thalamus also is removed, leaving part of the subthalamic structures and the whole midbrain intact. These preparations differ in but a single respect, namely, in the retention by the 'thalamus' animal of normal temperature regulation, which the 'midbrain' animal has lost. Although both these preparations are deprived of their cerebral hemispheres, yet they differ in a remarkable manner from the 'decerebrate' animal with which we have so far been dealing. When the operation is completed, the animal (rabbit) is laid upon its side, and as it recovers from the anaesthetic it gradually rises to a squatting position, head first and the neck and trunk slowly righting themselves until the animal sits erect in a natural posture. The distribution of tone in the musculature is what Magnus describes as 'normal'. There is no extensor rigidity, and both extensors and flexors exhibit, as demonstrated by passive manipulation of the limbs, tone of normal intensity. A great variety of reflex reactions can be elicited in these preparations. All the normal nutritional reflexes are intact. When the optic nerves and tract are preserved, pupillary light and blinking reflexes are obtainable. Numerous pseudaffective reflexes occur. In the rabbit, passive movements of the eyes evoke no modifications of posture, hence in this animal no postural proprioceptive reflexes arise in the eye-muscles. In this respect, as we shall see, monkeys differ strikingly from lower species. Left to itself the thalamus or midbrain animal remains motionless, but it can be stimulated by auditory or cutaneous stimuli to movement—walking, running, or jumping. All these are carried out in a normal manner with perfect co-ordination, and when they cease the animal resumes its sitting position. If overturned it rights itself at once, and, in whatever position the animal be placed, the head at once resumes the upright normal posture. In short, all the postural reactions of the intact animal have been found to be present in these preparations. The sum total of all these reflexes, Magnus designates '*postural reflexes*'

(*'Stellreflexe'*), as opposed to the tonic reactions described in the preceding section which he groups together as 'standing reflexes' ('Stehreflexe').

Analysis of the 'Stellreflexe' reveals four component groups:

(1) Labyrinthine reflexes acting upon the head.
(2) Reflexes arising in the body-wall and acting on the head.
(3) Reflexes arising in the neck-muscles (secondary to (1)).
(4) Reflexes acting on the trunk and limb musculature.

(1) *Labyrinthine reflexes acting upon the head* ('Labyrinthstellreflexe auf den Kopf'). Their function is to right the position of the head in space. They are best studied by holding the animal in the air. In whatever position this be done, the head at once rights itself. The righting involves rotation of the neck, and thus (3) *secondary neck reflexes* ('Halsstellreflexe') are set up which bring the trunk into line with the head. After bilateral extirpation of the labyrinths, and as long as the animal is held in the air, the head cannot be righted, and secondary neck reflexes also fail to arise. However, directly the animal is placed in contact with the ground, or some other flat surface, even after loss of both labyrinths, the head is at once righted, secondary neck reflexes follow, and the neck and trunk come into line with the head. This is due to (2) *reflexes arising from asymmetrical stimulation of the body-wall* ('Stellreflexe auf den Kopf durch asymmetrische Reizung der Körperoberfläche'). If the animal be laid on its side, the pressure caused by its superincumbent weight acting on the lower surface gives rise to an asymmetrical stimulation of pressure sense nerve endings. A reflex response righting the head results. That this explanation is correct, Magnus has demonstrated by an ingenious experiment ('Brettversuch'). A flat board is laid upon the upper free body surface supporting a weight. In this way the stimulation is rendered symmetrical and the head at once sinks on to the floor, to remain there until the board be removed. We see, therefore, that the righting of the head depends upon impulses arising in the labyrinth when these are asymmetrically placed in relation to the horizontal plane, and by reflexes arising from asymmetrical stimulation (cutaneous or subcutaneous) of the body-wall. By means of neck reflexes secondarily set up, the trunk follows the head. Therefore trunk posture depends upon that of the head. As the animal recovers from the operation (removal of hemispheres) these reflexes can be seen to come into action one after the other. First the head rises (labyrinth reflexes). This causes rotation of the neck and secondary neck reflexes follow, and the trunk from before backwards gradually assumes the upright position. However, the intact animal can maintain its head in a variety of asymmetrical positions without the body following it and causing the animal to overbalance. Therefore a further group of 'Stellreflexe' must be present in normal life. This is the group of (4) *reflexes acting upon the limbs and trunk from asymmetrical stimulation of the body surface* ('Stellreflexe auf den Körper durch asymmetrische Reizung der Körperoberfläche'). If the head of the sitting thalamus animal be rotated laterally through a right angle, the body follows into the lateral position, but once this is reached, the body rights itself immediately and regains the normal position, although the head be maintained in the asymmetrical posture. Repetition of the 'Brettversuch' shows that this reflex also arises from pressure on one body surface. There is therefore direct provision for righting the trunk irrespective of the position of the head. Of the four groups of 'Stellreflexe', therefore, two are concerned in the righting of the head, and two in that of the trunk.

In the decerebrate animal all four groups of 'Stellreflexe' are absent. Hence it is clear that the centres concerned lie in the midbrain cephalad to the plane of the posterior corpora quadrigemina. They persist after ablation of the cerebellum, and their afferent and efferent paths cannot, therefore, pass through this organ.

Observations on normal animals show that the tonic labyrinthine and neck reflexes and the postural reflexes ('Stellreflexe') are the sum total of all the postural reactions of the intact animal. The description we have briefly given of the latter groups is taken from Magnus's observations on the rabbit, but they have been repeated in the cat, dog, and monkey. The principal difference between the first and last of the series is the presence in the monkey of an important group of 'Stellreflexe' arising in the eye-muscles. They are totally lacking in the rabbit, in whom the eyes play no part in postural regulation. In the monkey, on the other hand, the eyes can replace, or can fully and rapidly compensate for, loss of both labyrinths. Thus, after bilateral ablation of the labyrinths, the monkey soon becomes able to right the head when the animal is held in the air, if it be allowed the use of vision. Once the eyes are blindfolded, complete inability to orientate and right the head returns.

Finally, many of these reflexes have been demonstrated in the new-born child and in patients with nervous lesions more or less equivalent to functional loss of the cerebral hemispheres (hydrocephalus, meningitis, ventricular haemorrhage). Therefore we may safely apply the fruits of these researches to clinical problems, remembering the complicating factor introduced by the assumption on the part of man of the upright posture and the variation which this involves in the setting of the head upon the trunk.

It is clear that such a vast amount of experimental research, involving as it does so many new conceptions and terms, and being so rich in results, can be dealt with in but summary fashion within the scope of this review, and only the most salient features have been referred to here. Many eye reactions have not been touched upon at all, and no mention has been made of a group of reflexes (dynamic reflexes, 'Bewegungsreflexe') brought into being by actual movement (rotation and movement in a straight line). These we hope to deal with in a subsequent review. Suffice it to say that they arise in the semicircular canals, and not in the otolith organs, which are the source of all the tonic labyrinthine reflexes which have been discussed in these pages. We have dealt with but a single side of the problem of co-ordination of movement and the maintenance of equilibrium, namely, the postural side, and the point we now emphasize is that muscle-tone is the basis of all these reactions ('Reflexe der Lage', or static reflexes).

Magnus and de Kleijn have also attempted to analyse in detail the function of the otolith organs and apportion between the maculae of the utricle and saccule respectively the different labyrinthine reflexes. They find that the maximal position of labyrinthine influence on the extensor tone of the decerebrate animal corresponds to that position in which the otoliths of the macula in the utricle are dependent from the macula. Conversely, the minimal labyrinthine influence obtains when the otoliths rest upon, or press on the macula. These facts have been determined by the construction of wax models of the labyrinths from serial sections of these organs.

Apart from the great interest of this work considered from the point of view of experimental physiology, it has a further double importance for the clinical neurologist. Already many of the reflexes in question have been identified in man, and, further, we may note that *of all the motor functions which it is now the fashion to localize in the corpus striatum, there is scarce one which has not been conclusively shown by Magnus to be primarily a function of centres situated in the midbrain.* Whatever value the corpora striata may possess as superimposed and controlling centres, it is clear that the essential nervous mechanism for the maintenance and regulation of muscle-tone, the co-ordination of posture, and the performance of what have been called automatic and expressional movements is contained in the brain-stem between the cephalad limits of the midbrain and the plane of the calamus scriptorius caudally. We have only to consider the somewhat similar case of the cerebellum to realize that this is not to deny postural and other motor functions to the corpus striatum. We have seen that neither the centres concerned in the reactions we have been considering nor their afferent or efferent paths come within the compass of the cerebellum, that ablation of this organ *in an animal newly deprived of its cerebral hemispheres* does not impair a single one of these reflexes. Nevertheless, when the forebrain is intact and active, cerebellar lesions, as experimental and clinical observations have amply proved, give rise to gross disorders of co-ordination in voluntary movement. These disorders we can with confidence trace to loss of tonic postural reactions, once we adopt the modern conception of muscle-tone (cf. *Brain*, 1921, **44**, 539). In other words, for the *simple reflex activation* of the postural brain-stem centres, the control or intervention of the cerebellum appears not to be essential. It seems probable, however, that in the *voluntary* (*cerebral cortical*) *activation* of these motor mechanisms the cerebellum is necessary, that the cerebral motor cortex acts upon them through the medium of the cerebellum and not otherwise. Arguing from this analogy, we may suppose that while the mechanisms we have been considering are entirely outside the corpus striatum and can be reflexly thrown into perfect activity without its co-operation, yet, when voluntary motor innervation is in question, the corpus striatum may occupy a physiological position somewhat similar in general principle to that we have postulated for the cerebellum. Hence destructive lesions of the basal ganglia may be the cause of abnormal activity on the part of the midbrain postural centres. It must be admitted that the phylogenetic history of the two structures and their fibre connexions are very different, so that the analogy must not be pressed too far. Finally, while it may be objected that the hypotheses now tentatively advanced are no less speculative than those we have felt bound to criticize, yet they appear not to conflict with clinical experience and they do not run counter to well-established facts of experimental observation.

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F. M. R. W.

THE D'HÉRELLE PHENOMENON

Introduction. This phenomenon, brought into prominence by the researches of d'Hérelle, and therefore frequently associated with his name, has revealed, in his opinion, the existence of an ultra-microscopic organism, small enough to pass through a Berkefeld filter, that lives as a parasite upon living bacteria and is widely distributed in nature. As a result of its parasitic action bacterial changes are produced. Prominent among these is lysis, evidenced by clearing of a bouillon culture in which the 'microbe bactériophage', as he has termed the parasite, is growing. Lysis, as well as other bacterial changes, can be effected in a second culture by adding a few drops of Berkefeld filtrate from the first; and this can be repeated indefinitely. An impression of growth of the parasite was thus obtained.

d'Hérelle's opinion has not, however, received universal support. That a living parasite is in operation has been called in question. The bacterial changes characteristic of the phenomenon are without doubt initiated by some obscure substance which has been obtained from very diverse sources —for example, from intestinal contents, sewage, soil extracts, leucocytes. Further, the phenomenon having been once started, a substance can be demonstrated which increases in the presence of living bacteria, and to which obviously the bacterial changes must be attributed. The nature of this substance is, however, controversial. Whatever it may be, the study of its action has shown that some aspects of bacterial metabolism, bacterial variation, and virulence are fundamentally involved, and the question arises as to whether the active principle itself is a living parasite, an enzyme, or an enzyme-like substance with the power of growth.

Twort (1915), in a paper entitled 'An investigation on the nature of ultra-microscopic viruses', described a peculiar change that occurred in colonies of micrococci cultured from vaccine virus. In agar tubes incubated at 37° C. for 24 hours some colonies were found that could not be subcultured, and if kept they became glassy and transparent. When this glassy material was stained it showed only minute granules. If a pure culture of the micrococcus was touched with a portion of the glassy material the growth at that point became transparent and the change spread gradually to the surrounding culture. This glassy substance was still active when diluted one part in a million and passed through the finest porcelain filters. It acted best on young cultures; on cultures killed by heat it had no effect. Inoculated on agar without micrococci it gave no sign of growth, but retained its activity for over six months. It resisted heating at 52° C., but was destroyed by 60° C. for one hour. The action was most marked on the white and yellow micrococci cultivated from the vaccine virus, was much weaker on *Staphylococcus aureus* and *albus*, and there was no effect on members of the intestinal group, streptococci, *B. tuberculosis*, or yeasts. In old cultures in which the glassy material had not destroyed all the micrococci, these would commence to grow again and would overspread the glassy substance although the latter was shown to be active by its effect on a new culture. Similar findings were obtained with a micrococcus and a member of the intestinal group from the mucous membrane of a dog suffering from distemper; also from cases of infantile diarrhoea.

In making deductions about the nature of the glassy change, he says, speaking of vaccine virus, 'on the whole it seems probable, though by no means certain, that the active transparent material is produced by the micrococcus'; also, 'it is clear that the transparent material contains an enzyme and it is destroyed at 60° C.'; again, 'it also increases in quantity when placed on an agar tube containing micrococci obtained from vaccinia, and this can be carried on indefinitely from generation to generation', and, 'the possibility of its being an ultra-microscopic virus has not been definitely disproved, because we do not know for certain the nature of such a virus'. He suggested that the phenomenon would be found in cases of dysentery and allied conditions.

d'Hérelle (1917), without the knowledge of Twort's work, published the first of a long series of notes on the subject of a 'microbe bactériophage' which, he believes, is a living filterable organism that is parasitic upon bacteria, and which he obtained in the first instance from the intestinal contents of a patient with dysentery. The action of his 'microbe bactériophage' upon bacterial growth made it evident that both he and Twort were dealing with the same phenomena. Such appears to be the logical conclusion, and it is held by many who have studied the subject, Fildes (1920), Bordet (1921, 4) Gratia and Jaumain (1921, 1), although d'Hérelle (1921, 1) himself does not agree in this opinion.

As a result of d'Hérelle's articles, interest in the subject was aroused, and from that time there has been a continually increasing literature. In a general way many have observed the same phenomena, but the interpretation of experimental results leading to conceptions of the nature of the causative agent have been vastly different. Twort (1915) was content to make several suggestions, but settled upon none. d'Hérelle, from the commencement of his publications, has maintained that the active agent is a living filter-passing 'microbe bactériophage'. Bordet (1921) believes that it is an autolytic enzyme produced by the bacteria. Kabéshima (1920, 2) looks upon the active agent as a catalyst that causes micro-organisms to produce autolytic ferments, these in their turn acting as catalysts to other micro-organisms, the catalyst originally coming from the patient with dysentery as a protective measure against infection. Salimbéni (1920, 2) reports having demonstrated a myxamoeba in samples of the active substance, and advances this as the causative agent. Bail (1921, 1) suggested that under some non-determined influence the bacteria break up into particles small enough to pass through a filter. These particles will not live in a bouillon culture alone, but if associated with normal organisms they will not only live, but multiply, and may to some extent regenerate. Otto and Winkler (1922) expressed similar views. Their results suggested to them that the active substance was not an invisible microbe, but that it was made up of minute fragments of bacterial protein with fermentative properties, which arise from the destruction of bacteria, and that it resembled the autolysates of living bacteria.

The confusion that exists regarding the nature of the active principle is indicative of the uncertainty that exists at present about the interpretation and significance of the phenomena resulting from its action, phenomena relating to bacterial growth, destruction, and variation: phenomena which up to the present have been collectively termed in the literature ‘the d'Herelle phenomenon’, ‘the Twort-d'Hérelle phenomenon’, ‘le bactériophage de d'Hérelle’, or ‘l'autolyse microbienne transmissible’. A discussion of the theories relating to the active principle itself may, for the purpose of this summary, be temporarily set aside. Its exact nature is at present undetermined, but eventually the question of what it is must become of fundamental importance. Throughout this paper it will be termed simply the ‘active substance’.

In reading the literature it is somewhat difficult to form a comprehensive and systematic conception of the subject, and for several reasons. The fact that a difference of opinion exists about the nature of the active substance is in part responsible. d'Hérelle takes his stand upon a ‘microbe bactériophage’ and interprets all his results to maintain the idea. Bordet and Ciuca, Gratia, Wollstein, Kabéshima, and others, do not believe that the active substance is a living organism, and have experimental results to confirm their opinions. Both d'Hérelle (1921, 1) and Bordet (1921) have given a systematic exposition of their views, as wide apart as their conceptions of the nature of the active substance. It is proposed here to review the subject under arbitrary headings.

The origin of active substance. Although the ultimate origin of the active substance is unknown, it is possible to connect all the sources from which it has been obtained with animal cells. That it has any connexion with plant cells has not been demonstrated. Bordet and Ciuca (1920, 1 and 2) derived their samples from peritoneal exudate in guinea-pigs after injecting *B. coli communis.* Twort (1915) found the substance in vaccine virus, in the intestinal mucous membrane of a dog with distemper, and the intestinal contents of a child with diarrhoea. d'Hérelle (1921, 1) obtained it from the faeces of patients with dysentery, from the urine and faeces of a patient with typhoid fever, and also from the stools of healthy people. He found it in sea-water at Marseilles and Alexandria (d'Hérelle 1922, 2) and he believes it is normally present in the intestine of many species, for he also found it in the manure from 26 horses and in the dejections of hens, monkeys, cats, cattle, buffaloes, pigs, rabbits, and goats. Dumas (1920) obtained it from the faeces of healthy guinea-pigs, from samples of earth, from the contents of a sewer, and from the Seine. Lisbonne, Boulet, and

Carrère (1922) produced a sample by mixing leucocytes with *B. dysenteriae* (Shiga) *in vitro.* This confirms Bordet's opinion that the leucocytes are the ultimate origin of the active substance. But, on the other hand, d'Hérelle (1922, 2) states that the 'microbe bactériophage', far from being produced by leucocytes, is phagocyted and destroyed by them, and in this he is supported by Bruynoghe and Maisin (1922, 2). Kuttner (1921, 2), by extracting the small intestine and the liver of healthy guinea-pigs with glycerine, obtained a substance active against *B. typhosus.*

The effect of active substance on bacterial cultures. The presence of active substance is detected by the effect it has on cultures. The effect that first attracted the attention of d'Hérelle was clearing. If a small amount of active substance is added to a young culture of an appropriate organism in bouillon and placed at 37° C., the cloudiness decreases and in a few hours the culture becomes clear, the result of lysis. After a varying time it again becomes cloudy.

If a drop is taken from a mixture of young bouillon culture and active substance, immediately after the active substance has been added, or later, and spread over a plain agar slant, which is placed at 37° C., a characteristic appearance will develop that varies according to the strength of the active substance.[1] If the substance is strongly active the agar surface may be completely devoid of growth except for one or two colonies of normal appearance. A lesser degree of activity is denoted by a growth partially covering the surface, showing a ragged, frayed out, moth-eaten contour, or it may be broken up into small irregular patches by the barren areas. A still milder activity produces a growth covering the whole surface, but spotted with small circular barren areas varying in size from less than 1 mm. to 2 or 3 mm. These areas are termed 'plages' by d'Hérelle. In the tube showing only a few normal colonies and in the tubes with irregular islands of growth, the barren areas are not completely bare. One finds there more or less of a delicate greyish substance in small patches, very irregular in size and shape, spread out in feathery processes. It has a dry lustre and does not give one the impression of bacterial growth.

If one inoculates an agar plate it is possible to observe the effect upon isolated colonies. The changes are similar. A few colonies appear to be normal; the majority have a scalloped periphery and may be markedly deformed. There are many that could hardly be termed colonies because they are only remnants left from the deforming process.

The delicate greyish substance with the dry lustre, described above, may also be seen on the plate. It appears between colonies, it surrounds in feathery processes the small remnants of colonies, and to a lesser extent is seen along the scalloped edge of colonies less deformed. It will not grow if transferred to a fresh culture. When stained it is granular and amorphous, with an occasional granular or swollen organism.

The same changes may be observed if a drop of active substance is spread over the surface of an agar slant, followed immediately by a similar inoculation with a young bouillon culture. It is not essential that the two should be mixed before inoculating the agar.

If active substance is added to a freshly inoculated bouillon culture the medium remains clear for much longer than a control tube without active substance, but eventually becomes cloudy.

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[1] For illustrations see Maitland (1922).

All of these effects can be explained by two properties of the active substance, lysis and inhibition, which will be discussed in more detail in a later section.

Isolation of the active substance. Active substance has been isolated from many sources. It has never been known to develop spontaneously in a culture. In every instance some material—filtrate of a faecal culture, soil extract, sea-water, peritoneal exudate, leucocytes, &c.—has been put in contact with living bacteria and active substance has developed. An exception may be made of Otto and Winkler (1922), who believe that active substance consists of fragments of bacterial protein and that the phenomenon can be initiated or intensified by producing bacterial injury, either by mechanical or chemical means. Twort worked with growth on agar. Every one else, for the purpose of isolating samples of active substance, has used bouillon cultures. An isolated sample of active substance has therefore consisted of a Berkefeld filtrate of a bouillon culture in which active substance has been produced (d'Hérelle) or a similar bouillon culture in which the bacteria have been killed by heat (Bordet and Ciuca). The technique of these workers will be mentioned as representative.

The technique of d'Hérelle (1918, 1) and (1921, 1) is as follows: a few loopfuls of faeces are put in a tube of bouillon and incubated overnight at 37° C. The culture is filtered through a Berkefeld or similar filter. A few drops of the filtrate are added, for example, to a young culture of *B. dysenteriae* (Shiga) in bouillon and placed at 37° C. A clearing of the culture would indicate the presence of active substance, but if the clearing is slight or uncertain the active substance may be more certainly detected by transferring a drop of the culture to an agar slant and incubating it for 18 to 24 hours. Bare spots would indicate active substance. The Berkefeld filtrate of such a culture would be a sample of active substance. Other cultures, if desired, may be substituted for *B. dysenteriae.*

Bordet and Ciuca (1920, 1 and 2) isolated their samples by injecting *B. coli* into the peritoneal cavity of guinea-pigs, three injections at five-day intervals. One day after the last injection the peritoneal exudate, which contained a few living bacteria, was added to two or three volumes of sterile bouillon and kept at 37° C. for 8–24 hours. It was then heated at 58° C. for 30 minutes, diluted with several volumes of bouillon, and inoculated with a drop of a fresh culture of *B. coli.* This was incubated for one day and left at room temperature for two or three days. It was again heated at 58° C. for 30 minutes and found to contain the active substance. Such a culture or a Berkefeld filtrate of it would constitute an isolated sample of active substance.

Increase of active substance in a bouillon culture. If a few drops of the filtrate from a cleared bouillon culture are added to a second young culture in bouillon, it too will become clear, and this can be repeated indefinitely. d'Hérelle (1921, 1) carried it through more than nine hundred transfers. There is no doubt, therefore, that active substance increases in bouillon when associated with living organisms. This conclusion is obviously correct although deduced indirectly. It was necessary to conclude that the active substance had increased, for its action was still apparent after such a large number of dilutions. It has, however, been shown (Maitland, 1922) that increase can be demonstrated by direct measurement and that an increase of active substance does not necessarily imply a lytic action on the culture in which it is produced.

Active substance will not increase in bouillon alone, nor in bouillon with dead bacteria. If a filtrate containing active substance is inoculated on an agar slant it does not increase, nor is there any visible change in the agar.

The properties of active substance. According to d'Hérelle (1921, 1) a freshly isolated sample of active substance is destroyed by heating at 68° C. for one hour, but a sample two weeks old is not destroyed by this exposure. He attributes the difference to the formation of spores by the 'microbe bactériophage' while it is not in contact with living bacteria. In a later article (d'Hérelle and Pozerski, 1921), using an improved technique, he states that the 'bactériophage' is attenuated more or less rapidly when heated above 60° C., but is not totally destroyed until 75° C. is reached. Twort's samples from vaccinia were destroyed at 60° C. According to Bordet's technique, heating at 58° C. for 30 minutes kills the bacteria, but not the active substance, which is destroyed at from 60–65° C.

d'Hérelle (1921, 1) has recorded the following observations on the length of time the activity may be preserved. Filtrates have been found active after six years, having been kept in a sealed tube. Slow evaporation to a syrupy consistency at room temperature is not destructive. A piece of sterile filter-paper impregnated with an active filtrate dried *in vacuo*, and kept for six months in a sealed tube, has retained the activity of the filtrate. This paper added to a young culture caused lysis. Four samples of faeces kept in sealed tubes yielded active substance after thirty-four months.

With regard to chemical agents several observations have been made. Eliava and Pozerski (1921, 2) found that hydrochlorate and acid-hydrochlorate of quinine were totally destructive in a concentration of 0·75 to 1·0 per cent., and that with the same technique carbolic acid and sodium fluoride were harmless in amounts of 2·5 per cent. Bablet (1920) records a destructive action of solium fluoride in amounts of 1 per cent., also that chloroform will abolish the activity. Contact with glycerine for eight days rendered the substance inactive; but d'Hérelle kept a sample in equal parts of glycerine and bouillon, or glycerine and saline, for two years. d'Hérelle found that active substance could be left in contact with bichloride of mercury, 1 in 200, copper sulphate 1 in 100, or carbolic acid 1 in 100 for three days, without loosing its activity, but after four days, in the case of bichloride of mercury and copper sulphate, and after seven days with carbolic acid, its activity had been destroyed.

Applemans (1921, 2) found that contact with 50 per cent. alcohol for twenty days, or 5 per cent. carbolic acid for eight days, rendered the substance less active but did not destroy it. It was, however, destroyed by exposure to ultra-violet rays for ten minutes (Applemans, 1922).

Kabéshima (1920, 2) gives the destructive temperature as 75° C. His experiments with regard to the action of chemicals are very striking. To an active bouillon filtrate he added three volumes of acetone, and let it stand for 48 hours. He then evaporated and obtained a yellowish-white powder that was much more active than the filtrate itself. The lysis produced by the powder was carried through 408 passages. The powder did not lose its activity after several weeks' contact with pure acetone, but after ten weeks its power diminished.

A second procedure was to add to the bouillon filtrate an equal volume of anhydrous ether. After standing 48 hours he removed the ether layer, evaporated it, and obtained a waxy residue which contained active substance. He also noted (1920, 3) that it resisted the action of chloroform, toluol, and carbolic acid. From his results he concluded that active substance must be a ferment, but d'Hérelle (1920, 3) replied that the conclusion was not warranted, that the 'microbe bactériophage' was endowed with a resistance comparable to spore-forming bacteria.

The effect of active substance on bacteria. The effects of active substance on bacterial cultures have already been noted; but a change produced in a culture is a rather gross manifestation of its action, an expression of activities that have been applied to all the organisms individually. A study of the effects of active substance on bacterial cells is therefore much nearer the root of the problem.

The clearing action in bouillon cultures has already been mentioned, and it has been generally observed that if a cleared culture is allowed to remain in the incubator it again becomes cloudy. The cloudiness reappears because not all the bacteria have been destroyed. It is due to a multiplication of the organisms that have resisted lysis. Thus a distinction is made; some organisms are resistant, some are susceptible to lysis.

Another manifestation of resistant organisms is seen in the colonies, of normal appearance, that are to be found on the surface of agar inoculated with active substance and bouillon culture. These colonies may be the only growth. If such a colony is subcultured it will yield a strain that will not be acted upon by active substance. Such a resistant strain resembles a normal culture in all superficial respects. It differs in resistance to the active substance. In both broth and agar resistant organisms have been recognized because they grow after contact with active substance.

The essential difference between organisms that are lysed, and those that resist, is not fully understood. Such differences have been shown to appear spontaneously in a culture that had not been exposed to active substance. Gratia (1921, 3 and 8), working with a normal culture of *B. coli* started from a single colony, was able to isolate two types which he designated 'S and R', or 'sensitive' and 'resistant'. These types were obtained by subculturing colonies that showed slight differences in a culture which he had allowed to age. Type 'S' was sensitive to the active substance; it was susceptible to lysis. Type 'R' was much more resistant. They differed in other respects also. 'S' grew more quickly in an artificial medium, and was non-motile. 'R' grew more slowly and was very motile, was less phagocytable, and more virulent. Both types fermented the same carbohydrates, produced indol, and kept their individuality after passing through a guinea-pig. These, it may be repeated, were spontaneous differences found in a culture that had never been exposed to active substance.

Gratia (1921, 7 and 9; 1922, 2) carried farther the division of one culture into types. The agents of division were spontaneous variations and active substance. The differences looked for were differences in the appearance of colonies, differences in motility, and different degrees of susceptibility to the action of active substance. Working along these lines he was able to obtain eleven different varieties from the original culture. To what extent this remarkable analysis of one culture indicated fundamental differences is a matter upon which at present it is difficult to form judgement; but it does seem to indicate that there are individual differences in the organisms of one culture which relate to the activity of the substance under discussion.

In the analysis of his culture Gratia distinguished between organisms of a normal culture and resistant organisms that grew after the culture had been exposed to active substance. Varying degrees of susceptibility to lysis were found in both normal and resistant organisms, but it was permissible to make the distinction, because organisms that have been acted upon by active substance are altered in one respect at least; they are endowed with the property of producing active substance. This is the conception first suggested by Bordet and Ciuca (1920, 1 and 2), Bordet (1921), and since supported by Gratia (1922, 2), Kabéshima (1920, 3), and Wollstein (1921). According to d'Hérelle's theory (1920, 3, 4, and 5; 1921, 1) this is not so. Whether or not one accepts the theory, the observations upon which Bordet's conception is based are in themselves of importance. These go back to the growth on agar of a mixture of normal organisms and active substance. Some colonies, as has already been mentioned, are well formed and by all appearances are normal. Others are deformed in varying degrees, and those most severely deformed suggest only remnants of colonies. All are, however, resistant. Bordet and Ciuca (1920, 2) observed that a bouillon culture of resistant colonies in itself produced active substance, but he did not differentiate between normal and deformed colonies. Wollstein (1921) and Gratia (1922, 2) made this distinction. The colonies of normal appearance gave strains that were uniformly and completely resistant to active substance. Further, a bouillon culture of such a strain did not produce active substance.

It was the deformed resistant colonies that Bordet and Ciuca referred to as producers of active substance. When they are grown in bouillon, active substance appears; and although they are resistant colonies, because they have grown after contact with active substance, not all the organisms are completely resistant. If they are again mixed with active substance and inoculated on agar a growth will appear containing both well-formed and deformed colonies (Wollstein (1921)). It is supposed by Wollstein and Gratia that the deformity is an expression of a variable individual resistance of organisms in that colony. The colony is deformed because some organisms are susceptible to lysis. Wollstein (1921) further supports the conception, that organisms in a deformed colony are not all alike, with an observation that some completely resistant colonies will appear when growth from a deformed colony is mixed with active substance and inoculated on agar. She also observes that subcultures of deformed colonies revert to the wholly resistant type, the explanation being that since active substance is produced it acts upon the susceptible individuals of the culture and gradually eliminates them.

Bordet and Ciuca (1921, 1) found that a few organisms from a subculture of a deformed colony (as few as fifteen) added to a young bouillon culture would cause lysis, and they believe, therefore, that active substance must be produced by the bacteria.

Both Wollstein (1921) and Bordet and Ciuca (1920, 2) have noted that well-formed and deformed colonies did not differ in fermentation reactions.

This discussion has been concerned with the manner in which active substance emphasizes variations amongst individual bacteria in a culture, and with the evidence supporting the conception that some individuals are altered by contact with active substance in such a way that they commence to produce it. The effects that active substance exert on bacterial cells to produce the gross cultural manifestations of its action have not been mentioned. These manifestations are clearing and inhibition of growth.

When active substance is added to a young bouillon culture the resultant clearing must mean a destruction of bacterial cells. Lysis has occurred. The same conclusion is reached after observing the effect that a drop of active substance produces when allowed to flow over a delicate film of growth on a young agar slant. If the tube is kept at 37° C. in a few hours the track of the active substance will be indicated by a bare streak of agar. The organisms have been destroyed.

The inhibitory action is deduced from two observations. If a bouillon tube is inoculated and at the same time a few drops of active substance introduced, the culture will remain clear. After a varying period it will become gradually turbid, but growth is very markedly delayed, as compared with the control (Bordet and Ciuca (1920, 2) and Gratia (1921, 1 and 8)). Secondly, if the area of bare agar that indicates the track of active substance over a film of young growth is observed for a further period at 27° C. it will be found that some colonies appear. From Bordet and Ciuca's description (1920, 2) they are evidently deformed colonies. It may be recalled that Gratia and Wollstein attributed the deformity to varying resistance of the bacteria towards the lytic action. Bordet and Ciuca (1920, 2) explained it by suggesting that the active substance had an inhibitory action upon the growth of the colony.

Whether the deformity is to be explained by an inhibitory effect upon growth or by varying degrees of bacterial resistance to lysis can hardly be settled at present. There may not be, after all, a very great difference between the two expressions. An inhibitory effect upon growth would indicate that the organisms were more or less prevented from multiplying; a varying resistance to lysis, that more or less organisms persisted after they had multiplied. Thus by argument it is possible to bring inhibition and lysis to a point where their ultimate effects upon colony formation would be the same, and where it would be very difficult to distinguish between the two processes. For the present, however, the assumption seems to be warranted that active substance causes inhibition as well as lysis.

The various cultural changes must be but different aspects of these effects on individual bacteria. The graded appearance on the agar slants was obtained simply by using graded dilutions of active substance. The process that gave a tube almost devoid of growth must have been the same as the one that resulted in scattered 'plages'. The difference is only in amount of action. So, also, the deformed colonies must have resulted from the same process, since they were obtained with the same culture and the same active substance.

d'Hérelle maintains that all these changes are produced by the parasitic action of the 'microbe bactériophage'. The parasite destroys the bacteria. Each 'plage', he believes, represents one colony of the invisible microbe. This is the basis of his method for counting the 'microbes bactériophages'. The 'plages' are seen only when the active substance is dilute, and he cannot conceive of a diffusible ferment exerting a localized clearing action, such as would form 'plages'.

Gratia (1921, 4 and 8), however, has interpreted the large bare areas, the 'plages', and deformed colonies as expressions of variation in susceptibility of bacteria to the action of active substance. He believes that there are all grades of susceptibility amongst the individuals of one culture. When the active substance is dilute only the most susceptible organisms are lysed. Others slightly less susceptible commence to produce active substance, and the clear areas are therefore localized and scattered. He argues thus that a diffusible ferment can produce 'plages' and that it is not necessary to postulate a living invisible parasite.

Examination by dark-field illumination has not advanced the problem. d'Hérelle (1921, 1 and 3) reports small bodies that can be seen to enter an organism, multiply in it, and finally destroy it. These bodies are the 'microbe bactériophage'. Bordet and Ciuca (1921, 1), on the other hand, could see nothing to make them suspect a living parasite.

The relation of hydrogen-ion concentration. d'Hérelle (1921, 1) has stated that an alkaline reaction is necessary, that in an acid medium the phenomenon will not develop.

Gratia (1921, 1 and 8) determined the relation of hydrogen-ion concentration to the inhibition effect in bouillon. The retardation of growth was faint in reactions of P_H 6·8, 7·0, or 7·4, but much stronger in a more alkaline medium P_H 8·0 to 8·5. Between these extremes there was a gradation of effect, the inhibition becoming more pronounced as the alkalinity increased.

Antibodies for active substance. Bordet and Ciuca (1921, 3 and 5) were the first to study the immunity response to injection of active substance into animals. They inoculated rabbits with Berkefeld filtrates of cleared cultures of *B. coli* and studied the properties of the immune serum. A mixture of active substance and immune serum would not clear a culture of *B. coli*, nor prevent a culture from developing. If deformed colonies were inoculated on agar with immune serum they did not reproduce themselves as usual, but gave a growth of normal appearance. This growth transferred to bouillon also gave a culture of normal appearance, and did not spontaneously develop active substance as Bordet and Ciuca (1920, 2) had observed the bouillon cultures of deformed colonies to do. Thus the antiserum neutralized the inhibitory and lytic properties of active substance, and also removed the effects of its action from the organisms in a deformed colony.

A similar antiserum was produced by inoculating rabbits with organisms from deformed colonies, which was considered by Bordet and Ciuca (1921, 1) as indirect confirmation of their belief that these organisms produced active substance.

If a mixture of antiserum and active substance was added to a bouillon culture the active substance did not increase. Even when several passages to new cultures were made, so that the original amount of serum would be extremely dilute and ineffective, no increase was observed.

The antiserum was effective after heating to 58° C., complement was therefore not necessary. And one volume of serum neutralized ten volumes of active substance.

Bordet and Ciuca interpreted the results as evidence that active substance was not a living microbe. It was destroyed without complement. It was prevented from increasing by exposure to antiserum, even although the serum was later removed by dilution. d'Hérelle and Eliava (1921, 1) repeated the experiments with *B. dysenteriae* (Shiga). They produced a serum that acted in a dilution of 1–1,000,000. They criticized Bordet and Ciuca's experiments as being incomplete, and concluded from their own that the 'microbe bactériophage' was not destroyed. It was only inhibited temporarily, and after treatment with antiserum its usual action could be demonstrated. It was only delayed. They investigated the immune serum for 'sensibilisatrice' by the method of complement fixation. They found that a 'sensibilisatrice' was present, and that it was specific for the 'microbe bactériophage', no matter what its origin, nor upon what bacteria it had acted. They concluded that only one variety of 'microbe bactériophage' exists, that the samples derived from man and from animals are the same. The apparent differences in samples were in reality only differences in the 'virulence' of the parasite for different bacteria (d'Hérelle and Eliava (1921, 2); d'Hérelle (1921, 1)).

Maisin (1921, 3) found that the neutralizing effect of antisera was non-specific. He used two sera prepared against samples of active substance specific for *B. coli* and for *B. dysenteriae* (Shiga). Each serum neutralized both samples of active substance. Gratia and Jaumain (1921, 2) worked with two samples of active substance. One was active against *B. coli*, the other against staphylococcus. An antiserum for one would not neutralize the other. The neutralization was strictly specific. They pointed out, too, that a dilute antiserum would not completely neutralize active substance, but would inhibit its action for a time, thus accounting for a part of d'Hérelle's results.

Thus the study of antibodies has not tended to lessen the confusion. There is a general agreement that an antiserum can be produced. There is disagreement as to the nature and specificity of the antibodies. The study of complement fixation has been introduced, but conflicting results have been obtained regarding the specificity of the reaction. From these various results different opinions have been formed as to the similarity or dissimilarity of all samples of active substance. This is a fundamental point, and will be discussed further.

The similarity or dissimilarity of all samples of active substance. Bail and Watanabe (1922, 2) consider that stool filtrates contain not a single bactériophage but several. They state that from a single sample of filtrate several bactériophages can be isolated and propagated. The grounds on which their differentiation was based are, however, such that this conclusion must be received with caution.

d'Hérelle's views (d'Hérelle (1921, 1), d'Hérelle and Eliava (1921, 2)) upon the similar nature of all samples of his 'microbe bactériophage' have just been stated. He believes that all samples contain an identical microbe. Variations in bacteria acted upon he expresses as alteration in 'virulence' of the invisible parasite, and points out that this very non-uniformity is a characteristic of living cells. His conclusions were based, for the greater part, on the properties of an antiserum prepared by inoculating a rabbit with active substance from a culture of *B. dysenteriae* (Shiga). This serum contained a 'sensibilisatrice', and gave an equal fixation of complement with various samples of active substance.

Gratia and Jaumain (1921, 2) demonstrated a difference between active substance for staphylococcus and *B. coli*. The serum prepared against one would not neutralize the other. They concluded that the samples were different. Bruynoghe and Maisin (1921, 4) prepared two antisera against active substance that operated on staphylococcus. They found that both sera gave complement fixation with active substance for staphylococcus, *B. typhosus*, *B. dysenteriae*, and concluded, therefore, that all these samples were identical. Their complement-fixation tests agree with d'Hérelle that samples are identical. On the other hand, results from neutralization tests with their antisera showed an absence of cross-neutralization, which agrees with Gratia and Jaumain.

The first necessity in attempting to solve the problem as to whether or not all samples of active substance are identical is obviously to define the criteria that would be acceptable as indicating the identical nature of all samples. No one has approached the question in this way. Observations have been made on the thermal destruction point, the bacteria acted upon, neutralization by antiserum, and complement fixation, but an analysis of all the observations does not enable one to arrive at any conclusion that can be held with conviction.

The work with antisera brought out the interesting point that by complement-fixation tests one serum gave cross-reactions with many samples, but neutralized the lytic action of the homologous active substance only. The interpretation of complement-fixation reactions made with such an uncertain antigen should be approached with care, and it is possible that the method may prove to be not a reliable criterion of similarity of samples of active substance. If such an attitude is adopted the discrepancy between the results obtained by this test and those of neutralization has only a passing interest.

The neutralizing action may have a deeper significance than complement fixation. d'Hérelle, making neutralization tests with a high-titre serum, contradicted Bordet and Ciuca's observation (1921, 3 and 5), that a serum would neutralize, and stated that the effect was only inhibition. Gratia and Jaumain (1921, 2) suggested the difference might be due to varying concentrations of serum. With dilute serum they observed inhibition of lysis, but stronger serum completely neutralized the lytic activity of their samples. Bruynoghe and Maisin (1921, 4) confirmed the results of Gratia and Jaumain, and suggested a possible explanation for the difference between inhibition and complete neutralization.

Their explanation presupposes an acceptance of the hypothesis that active substance is a living 'microbe bactériophage', and is based on some observations made by d'Hérelle with regard to enzymes of the invisible parasite.

d'Hérelle (d'Hérelle (1921, 1), d'Hérelle and Eliava (1921, 2)) claims to have isolated a diastase from the 'microbe bactériophage'. The method was to precipitate a sample of active substance with nine volumes of alcohol at 96° C. After 48 hours' contact the precipitate was removed and dissolved in saline. This solution caused clearing of a culture, but it could not be carried on in series. He therefore concluded that the alcohol had killed the microbe and that he had extracted the principle by which the invisible organism acts. The principle, deduced from the method of separation, was considered to be a diastase. He also refers to it as a lysin, and defines it in another place (1921, 1, p. 112) as follows: 'I mean by lysin the total secretions of the "bactériophage", without presupposing whether it is a question of a single diastase or of a group of diastases, which is more probable.' The conception of the 'microbe bactériophage' acting by means of lysins it secretes has been employed by both d'Hérelle and Bruynoghe and Maisin to explain the action of antisera.

d'Hérelle's explanation is that lytic action is never completely abolished because antiserum never destroys the living parasite. It neutralizes the free lysin. When, therefore, active substance and antiserum are added to a bouillon culture clearing is inhibited until more lysin can be secreted by the 'bactériophage'. Bruynoghe and Maisin explain their results by supposing that when the antiserum is dilute it neutralizes the lysin and delays clearing, but when the serum is stronger it destroys the 'bactériophage' as well. They observed complete abolition of clearing. For Gratia and Jaumain the whole of the hypothesis is untenable because they do not believe that active substance is a living organism.

Thus, on the fundamental point, as to whether all samples of active substance are the same or not, it is impossible to arrive at a conclusion. A review of the literature has revealed a remarkable conflict of opinions, not only upon this point, but throughout the whole *résumé*. Unfortunately the investigation of the subject has too often taken the form of controversy, an effort to refute or establish some particular aspect of the phenomenon. The fact that so fundamental a matter as the nature of the active substance itself has been in dispute has tended to lead supporters of one or other theory in pursuit of evidence to sustain their opinions, and consequently much of the evidence that has been obtained has been presented in a controversial and conflicting manner. There has been a great deal of important and suggestive work, but there is a need for more intensive study of some fundamental questions, and for a more critical attitude in forming deductions, so that the problems this phenomenon presents may be put beyond the reach of controversy.

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H. B. M.

ABSTRACTS

SURGERY

Peck, C. H., and **White, W. C.** **Tumours of the breast.** *Ann. Surg.*, 1922, **75**, 641–51.

These experienced surgeons discuss a series of 331 personal cases of mammary tumour, of which 136 were benign and 195 malignant. They adhere wholeheartedly to the classification and pathology adopted by Bloodgood (*Arch. Surg.*, 1921, **3**, 445). Of the 136 *benign tumours and cysts*, 23 were single cysts, most of them the typical 'blue-domed' cyst of Bloodgood; the writers emphasize the belief that this disease has no relationship to malignant dangers and that it should never be treated by excessive and mutilating operations, which are to be regarded as indications of timidity in diagnosis and prognosis on the part of the surgeon.

Localized areas of cystic mastitis are treated by excision of a V-shaped wedge of breast tissue, to which access is gained through a curved inframammary incision; stress is laid on the importance of deep-buried sutures to prevent the formation of haematomata. For general cystic mastitis they make the 'Warren' incision below the breast, reflect the whole mamma upwards, and remove the whole gland from the deep surface; they avoid undue flattening by leaving enough subcutaneous fat to suture together as a pad under the nipple. (The abstractor believes that this submammary approach has protentialities of danger in a disease that is known to be sometimes a precursor of carcinoma.)

The authors now follow Bloodgood in treating papillary cystadenoma as a benign tumour, although they regard smooth-walled cysts containing blood as 'essentially malignant'. They now consider that blood-stained discharge from the nipple does not, in itself, indicate malignancy or demand operation, unless a tumour is palpable. (In this they differ from many English surgeons who regard sanious discharge from the nipple, even when no mass is to be felt, as too suggestive of the possible presence of an unfelt duct carcinoma or of a potentially malignant duct papilloma to be ignored with safety.)

Bleeding from the nipple occurred in 6 of their cases, viz. 2 of papillary cystadenoma, 1 of local cystic mastitis, and 3 of fibroadenoma.

The ordinary encapsulated fibroadenoma is quite innocent, but the non-encapsulated variety is regarded with suspicion, for many should be treated as malignant; some, however, can be classified as non-malignant after gross examination of the cut tissue and treated as benign. The writers insist upon the necessity for the presence of a trained pathologist during breast operations for the decision of such questions. There were three cases of tuberculosis in the series, all of which remained free from tuberculous disease after operation.

Malignant tumours. Of their 195 cases, four were sarcomas and the rest carcinomas. Of these patients, six died in hospital after operation; three died of embolism on the seventh, tenth, and fourteenth days respectively, one died of shock within twelve hours, one of wound sepsis on the seventeenth day and one of an exacerbation of pre-existing cardiac disease on the fourth day. 118 cases were followed; of these 59 are dead or alive with recurrences; 53 are alive and well, of whom 27 were operated upon more than 5 years ago. As regards operative technique; the whole breast was removed and the axilla dissected in all 195 cases. The thoracic portion of the pectoralis major was removed in 186; the pectoralis minor was excised in 71; the pectoralis minor was divided and re-sutured in 54; part of the rectus sheath was excised in 23.

During the last six or seven years these surgeons have preferred the transverse incision of Stewart for the following reasons: The scar does not encroach on the shoulder or arm; the axillary exposure is excellent; the lower flap is readily slid upwards so that closure of the wound is facilitated and skin-grafting is rarely necessary. They prefer to retain the pectoralis minor, either retracting it or dividing and re-suturing it, because they believe that it protects the axillary vessels from cicatrizing bands and reduces the incidence of oedema of the arm after operation. They follow Handley in removing much more fascia and muscle than skin. Their dissection is made from above and within, downward and outward, and removes the sheaths of pectoralis minor and serratus magnus. (It is, however, difficult to believe that the fascial sheaths of these muscles can be completely removed without ablation of the whole muscle; moreover, excision of the pectoralis minor is required if the glands along the vein high up in the axilla and in the subclavicular region are to be removed with certainty.)

Involvement of supraclavicular glands is regarded as a sign of inoperability. Here again they insist upon the presence of a skilled pathologist during the operation to aid, by naked-eye inspection and the examination of microscopic frozen sections, in the determination of the character of the tissue presented.

In eleven cases delayed radical operation was done, the interval being occupied in the examination of the tumour removed at the first operation. Although this is not regarded as an ideal procedure, the delay was not found to alter the prognosis in this small series of cases; the second operation should follow the first within a few days. The authors' two cases of Paget's disease were 'frankly malignant'. One case of sarcoma is alive and well nine years after operation. Post-operative X-ray treatment is now their rule, but the writers have not yet formed definite conclusions as to its value. In recurrent cases X-rays and radium are believed to retard growth and to increase comfort, but no cures have been seen.

The following facts are interesting as indicative of the relative values of some of the physical signs and suggestive of the stages at which the patients came to operation: In the series 57 cases had retracted nipples; 16 ulcers; 94 skin adhesions; 31 adhesions to deep muscles; 9 multiple nodules (late cases); 77 palpable lymph nodes; 109 had involvement of the lymph nodes as shown at the time of operation; 15 complained of pain and tenderness. There was only one male in the series. The authors find retraction of the nipple and adhesions to superficial tissues of great diagnostic value.

Of the 59 traced patients who have died or suffered recurrences, 48 had involvement of axillary glands at the time of operation and 11 had not. Of 53 now alive and well 17 had involvement of glands and 36 had not.

69 patients have been traced who were operated upon more than 5 years ago. Of these there are:

Dead or alive with recurrence		42
With axillary involvement at time of operation . .	33	
Without „ „ „ „ „ . .	9	
	42	
Alive and well		27
With axillary involvement at operation	10	
Without „ „ „ „	17	
	27	
		69

In these 69 cases there were:

Alive and well more than 5 years	39 per cent.
Alive and well more than 5 years (with axillary metastasis)	23 per cent.
Alive and well more than 5 years (without axillary metastasis)	65 per cent.

These figures correspond with those of Sistrunk and McCarty (*Ann. Surg.*, Jan. 1922). C. C. C.

David, C. Vernon. **Papillary cystadenoma of the male breast.** *Ann. Surg.*, 1922, **75**, 652–7.

The writer begins by emphasizing the great rarity (probably less than one per cent. of mammary tumours) of any form of neoplasm in the male breast, and by pointing out that nearly all that do occur are carcinomatous in type, the innocent tumours being exceedingly rare. He adopts Bloodgood's classification of cystic changes in the breast (*Arch. Surg.*, 1921, **3**, 445) and then recapitulates the characters of papillary cystadenoma. 35 per cent. occur before 50 years of age and 30 per cent. between 50 and 70. Only eleven cases have been discovered in the male breast, according to available records. The tumour is generally under or near the nipple, is rarely bilateral, and seldom forms a projecting mass. The average size is that of a walnut, but it may reach that of a fist. The tumour is circumscribed and, except in very old, thinned, neglected cases, is not adherent to the skin. Rarely it may fungate through the skin. Axillary glands are not usually enlarged. Discharge from the nipple is present in 75 per cent. of cases; it may be sanious.

This author, unlike the writers of the article abstracted above (Peck and White), believes that the condition is often a precursor of carcinoma and that, therefore, wide removal of the breast should be done. He then records a case of this disease in the breast of an old man 82 years of age. It had been present for 15 years, but had been removed, apparently inadequately, 11 years ago. He gives short notes of 11 cases of papillary cystadenoma of the male breast, abstracted from the literature. C. C. C.

Schneller, Julius. Erkrankungen der männlichen Brustdrüse. [**Mammary diseases in the male.**] *Arch. f. klin. Chir.*, 1922, **119**, 169–210.

The author discusses the subject at some length, and includes a large variety of diseases. He emphasizes the necessity of distinguishing closely between true gynecomastia, with true hypertrophy, and those cases of pseudo-hypertrophy due to fat. Gynecomastia in association with genital defects is to be regarded as due to loss of the internal secretion from the interstitial cells of the testicles. The author states that about 2 per cent. of all mammary cancers occur in males. (The impression of the abstractor is that the proportion is rather smaller.) It has been suggested that the rubbing caused by the wearing of braces is a causative factor of mammary carcinoma in males, but doubt is thrown on this theory. But it is apparently true that the right breast is more frequently affected than the left, and most men are right-handed and therefore subject the right breast to more friction from the braces than the left. C. C. C.

Lorenz, H., u. **Schur, H.** Unsere Erfahrungen über den Wert der Antrumresektion bei der Behandlung des Ulcus pepticum. [**Our experience of the value of antrum-resection in the treatment of peptic ulcer.**] *Arch. f. klin. Chir.*, 1922, **119**, 239–76.

Schur and Plaschke in 1915 compared the acidity of the gastric juice after gastro-enterostomy and partial gastrectomy and found it diminished to a much greater extent after the latter than after the former operation. This finding agreed with the experimental results of Gross and Krzysckowski on dogs, except that in this animal removal of the antrum diminishes the secretion of HCl in response to chemical stimulus, leaving untouched the secretory response to psychic stimulus. In man the HCl content of appetite juice is also diminished by antrectomy. In spite of this discrepancy, the analogy between clinical and experimental findings seemed so strong that Schur and Plaschke urged a full resection of the antrum in cases of ulcer showing hyperacidity. In 1918 Kelling confirmed Schur and Plaschke's findings and accepted their explanation, and in the same year Finsterer reported good results from antrum resection.

Since 1915 antrum resection has been the operation of choice for gastric ulcer at Lorenz's clinic at Vienna. In 1921 the cases were collected and a full examination of 55 patients was obtained (clinical examination, test, and opaque meals). Reduced tracings of the latter are given and the cases divided into two groups—that in which the whole antrum was removed (43 cases), and that in which some portion of the antrum was still present (12 cases). Incomplete removal of the antrum was due either to fear of interference with nutrition, afterwards found to be groundless, or to the necessity for speed introduced by the poor condition of the patients. Free HCl was found in 3 of the 43 cases of complete antrectomy, and in 11 out of 12 cases of incomplete removal of the antrum. The degree of acidity in the latter group appeared to vary directly with the amount of antrum remaining. Normal peptic activity could be demonstrated by the addition of N/10 HCl to the gastric juice in all but a small proportion of the cases. Clinically there were no cases with persistent ulcer pain after operation among the 43 in which the antrum had been removed. Among the 12 cases in which a portion of the antrum was left there were 7 with persistent ulcer pain of varying intensity, 3 of them being recorded as definitely bad results. In 10 of the 43 there were symptoms suggestive of deficient gastric capacity, with occasional attacks of colic and diarrhoea. In the latter, examination of the stools revealed no unusual residue of undigested food, and the authors do not consider that their material supports the view that after extensive antrum resection there is deficiency either of digestion or of sterilization of the gastric contents. Slight symptoms dependent on reduced gastric capacity occurred with increasing frequency in the series *pari passu* with the increase in the amount of stomach removed.

As the result of their experience the authors support strongly the removal of the antrum as a routine part of the operation of gastropylorectomy, and consider that it offers the best guarantee against recurrence of ulceration, either in the stomach or jejunum. Cases of jejunal ulceration following partial gastrectomy, which have been reported by Frisch, Mandl, and Denk, they consider to be due to insufficient removal of the antrum, especially as Denk reported a high post-operative acidity. They admit the difficulty of defining the limits of the antrum at operation, and point out the wide differences between individuals in the level at which the change from fundus to pyloric type of mucous membrane takes place.

They also discuss the comparative value of gastro-enterostomy and partial gastrectomy, but maintain their preference for the latter on the ground of the greater diminution of gastric acidity. In conformity with most current writers, they condemn local resection of ulcers and segmental gastrectomy on the ground of the poor late results given by these operations. E. K. M.

Schroder, C. H. Congenital obstruction of the duodenum. *J. Am. M. Ass.*, 1922, **78**, 1039.

This case deserves note because of its rarity. The infant suffered from projectile vomiting, visible peristalsis, a tumour in the pyloric region, and retention. Operation showed great dilatation of the first and second parts of the duodenum, but no definite cause was found. *Post mortem* the stomach, and especially the duodenum, were much dilated, the dilatation ending sharply immediately above the ampulla of Vater. There a thick diaphragm, composed of all coats of the bowel wall, reduced the lumen of the gut to a diameter of $\frac{1}{8}$th of an inch. Schroder points out that the only approximately certain way of diagnosing the condition from pyloric obstruction is by means of radiography after a barium meal, and that gastro-enterostomy affords the only chance of survival. C. C. C.

Walton, A. J. Primary jejunal ulcer. *Brit. J. Surg.*, 1922, **10**, 152.

Woman, aged 45, complaining of pain, late after food, for 19 years. Soft tender swelling in epigastrium. Opaque meal negative. At operation, a round ulcer, 3 feet from the duodeno-jejunal flexure—enterectomy. Free from symptoms $2\frac{1}{2}$ years later. Microscopic examination showed simple chronic inflammation. No tubercle. Wassermann negative.

E. K. M.

Richardson, E. P. Jejunal ulcer without previous gastro-enterostomy. *Surg. Gynec. & Obst.*, 1922, **35**, 1–10.

Richardson operated on a case of stricture of the jejunum due to the contraction of an annular ulcer, microscopic examination of which gave no evidence of neoplasm, syphilis, or tubercle. With the idea that such an ulcer might be analogous in its formation with peptic ulcer of the stomach and duodenum, he searched the scanty literature of the subject and collected in all 12 cases. The clinical records of these were, for the most part, too meagre to form the basis of a discussion of the aetiology of the ulcers, but enabled him to point out that the majority were found in males, and that perforation occurred in 10 out of the 12. It was never possible to exclude syphilis, a recognized cause of chronic ulcer of the small intestine.

E. K. M.

Calzavara, D. Cefalopancreatite cronica e steatonecrosi. [**Chronic inflammation of the head of the pancreas and fat-necrosis.**] *Arch. ital. di chir.*, 1922, **5**, 265.

Originally considered merely as secondary to cholelithiasis, chronic pancreatitis, limited to the head, is now recognized as a rare but definite entity apart from gall-stones, and apart from the granulomata. It may be due to ascending infection, to circulating toxins, or may gain access by the lymphatic path from the biliary tract. If primary, the spread may be in a reverse direction following on biliary stasis by compression of the duct by the swollen and indurated pancreatic tissue. Arnsperger and others consider the condition as one of intra-pancreatic lymphadenitis, but biopsies do not confirm his view. Diagnosis is difficult. Investigation of pancreatic functional efficiency is complicated by vicarious or supplementary action of other glands, and moreover, in the cases under review, only a part of the pancreas itself is affected. The site of 'pancreatic' colic is in the midline rather than to the right, with radiation to the mid-dorsal and left shoulder regions, but neither point is diagnostic. Robson says that vomiting is absent, but Quénu and Duval speak of it as more frequent than with stones and sometimes uncontrollable. Jaundice is generally intense and progressive, but may be intermittent and transitory. When distension of the gall-bladder is present it is still difficult to differentiate from that due to tumour of the head of the pancreas, of the biliary tract, or of the ampulla.

Treatment is straightforward. In the presence of gall-stones or marked cystitis it is better to do a simple cholecystostomy, even if only as a temporary measure. Otherwise, a cholecystenterostomy or a cholecystgastrostomy should be performed, the author's preference being for a union with the stomach as less likely to permit ascending infection.

The particular interest of the reported case, which made a good recovery, was the occurrence of multiple small areas of fat necrosis in the omentum, appearing as pinhead-size whitish spots, not unlike tubercles. Histologically examined, these presented central areas of necrosis with a surrounding zone of formed connective tissue, within which were one or more layers of large polygonal epithelioid cells, with ample protoplasm and large round nuclei. Similar cells spread outside the nodules into the surrounding fat, and there, insinuating themselves in columns between the fat cells, determined absorption of the fat and atrophy of the whole adipose tissue. Their fate appeared to be to become fibroblasts; at any rate there was no sign of regeneration of fat as had been suggested by various authors under the term 'atrophy with proliferation'. There was some simple granulation tissue with giant cells in the vicinity of the nodules, but the large epithelioid cells were analogous to, if not identical with, the polyblasts of Maximow or the large phagocytes of Metschnikoff.

E. R. C.

Cutler, E. C., and **Newton, F. C.** **Some experiences with the 'Meltzer-Lyon' test in gall-bladder disease.** *Surg. Gynec. & Obst.*, 1922, **36**, 146.

The 'Meltzer-Lyon' test consists in the instillation of a strong solution of magnesium sulphate into the duodenum through a duodenal tube. Meltzer found that under such circumstances the sphincter of Oddi dilates and bile is poured out into the duodenum and can thus be removed through the duodenal tube for examination. Meltzer has assumed that with the dilatation of the sphincter the gall-bladder contracts and that the tube will withdraw three different types of bile. The first, which is described as 'A' bile, is light in colour and comes from the common duct. The second, or 'B' bile, is dark-brown in colour and presumably comes from the gall-bladder. The third, or 'C' bile, comes from the hepatic ducts.

The clinical performance of the test has been described by Lyon, but the present authors show that in the carrying out of this test there are a considerable number of pitfalls. They believe that in every case it must be controlled by X-rays to make sure that the duodenal tube is in the correct position. They find that, contrary to the observations of Lyon, the fasting duodenal content is always bile-stained. There is considerable difficulty in distinguishing the three specimens of bile by their colour, but although there is difficulty they place the greatest reliance on this factor. Microscopical examination of the sediments, on the other hand, has proved of but little value. Bacteriological examination of the specimens has also proved unreliable, chiefly owing to the failure to obtain positive cultures.

They carried out a large series of investigations, which they divided into normal controls—7 in all—and these were shown clinically to have no disease of the gall-bladder. In 14 cases the test failed to obtain 'B' bile, thus indicating that there was some obstruction of the cystic duct. A subsequent operation revealed the fact that the test was correct in 10—that is, in 71·4 per cent. In 5 cases abnormal bile was obtained in the 'B' bile, the abnormality chiefly consisting of large quantities of very dark, often viscid bile. All cases came to operation and the test-findings were substantiated. There were a few cases in which very little bile was obtained, pointing to obstructive jaundice, and in all of these cases the patient was jaundiced.

They show that this test has been very largely used, but that there has been the greatest conflict as to its reliability, and they say that the basis of the test centres about whether the law of contrary or crossed innervation exists, in that the gall-bladder will contract when the sphincter of Oddi dilates. There is considerable doubt as to whether the gall-bladder has such a power of contraction.

The reported papers on the test are discussed. Their own observations lead them to believe that there is much to be proved before the 'Meltzer-Lyon' test can be of value in aiding diagnosis. It is by no means a simple test, and to be exact it requires X-ray apparatus, much time, repeated examinations on all cases, and elaborate bacteriological and cytological studies. Their own experiences have left them with the impression that the test is not of dependable diagnostic aid. With its use in treatment, except for a few rare cases, they have no experience. A. J. W.

Butt, A. P. Round-worm in gall-bladder. *Surg. Gynec. & Obst.*, 1922, **36**, 215.

A brief account is given of the life-history of *Ascaris lumbricoides*, and doubt is expressed as to whether an intermediate host is required or not. The author quotes Huber as having found 68 cases of invasion of the bile-ducts by this parasite, and other cases of calculi in the gall-bladder, which contained the ova or even small worms. Living worms in the gall-bladder are, however, extremely rare. Butt reports a case of a woman, aged thirty, who suffered with symptoms suggesting a cholecystitis. At operation the gall-bladder was opened and a live worm six inches long was removed. The patient made a good recovery and a year later wrote that she had passed many worms before the operation but none since. A. J. W.

Fisher, D. Splenectomy in Banti's disease, third stage. *Surg. Gynec. & Obst.*, 1922, **36**, 171.

The author gives a brief review of all the reported operations of splenectomy for various conditions, together with the functions of the normal spleen and the results of splenectomy. Detailed notes are given of a patient with a three years' history of abdominal pain, enlargement of the spleen, and slight jaundice. The Wassermann reaction was positive. In spite of anti-syphilitic treatment the abdominal tumour increased in size and the jaundice persisted. Haematemesis set in and later, ascites. Splenectomy was performed, and at the same time the liver was noticed to be hypertrophied and the edges and surfaces hobnail in appearance. The gall-bladder was negative. After operation the general condition rapidly improved, the jaundice and ascites disappeared, and the patient was able to go back to normal work. There has been no return of the haematemesis and no epigastric pain, but the lower edge of the liver is still palpable. A second case is reported with a four years' history of pain in the abdomen and a tumour on the left side. This was followed by haematemesis and ascites. An operation upon the spleen was at first refused, but later the ascites increased and a splenectomy was performed. The liver was found large and cirrhotic. The patient failed to recover from the operation. A. J. W.

Bull, P. Early operation in appendicitis. *Norsk Mag. f. Lægevidensk.*, 1922, **83**, 7.

Since 1904, Bull has operated on 259 cases of acute appendicitis in his private practice. There have been 16 deaths, a mortality of 6·18 per cent. In the first group, covering the period 1904–8, there were 25 cases with 6 deaths. In the second group, covering the period 1908–15, there were 138 cases and 10 deaths, and in the third group, covering the period 1915–21, there were 96 cases and no deaths. Thus, in 15 years, the mortality was reduced from 24 per cent. to 0. This amazing change for the better was primarily due to cases coming to operation more and more early. In the first group 36 per cent. were operated on before, and 64 per cent. after, the 48th hour. In the third group these figures were respectively 81 per cent. and 19 per cent. The credit for the reduction in the mortality is, therefore, largely due to practitioners who, in the period under review, have come to realize the importance of sending a case early to the surgeon. An analysis of the severity of the cases in the three periods told the same tale. In the first period there were no slight cases, and there were 18 severe to 7 moderately severe cases. In the third period the percentage of slight, moderately severe, and severe cases was 37, 29, and 34 respectively. The conclusion to be drawn is that the earlier an operation is undertaken the less frequent will be the occurrence of severe cases. C. L.

Olivecrona, H. An experimental study of the circulatory failure in peritonitis. [**B.**] *Acta Chir. Scand.*, 1922, **54**, 559.

Since the publications, in 1899 and 1900, by Romberg, Pässler, and Heineke it has been generally accepted by surgeons that the heart is not primarily concerned with the circulatory failure in peritonitis, and that the essential feature of this failure is paralysis of the vasomotor centre caused by the direct action thereon of toxins absorbed from the abdominal cavity. Olivecrona has investigated this matter by determining the volume of plasma and of blood in 23 rabbits, 22 cats, and 6 dogs. The technique was essentially that of Hooper, Smith, Belt, and Whipple, but smaller quantities of brilliant vital red were used. The plasma- and blood-volumes were determined, as a rule, at least twice in each animal under normal conditions. Peritonitis was then induced, and the animals were examined in different stages.

It was found that there is in peritonitis a constantly occurring, and in the later stages, marked reduction of the plasma- and blood-volumes, which begins early, long before there is a serious fall of the blood-pressure or any decrease of the vasomotor reflexes. In most cases, not only was the blood-pressure normal, or nearly so, but the excitability of the vasomotor centre showed no appreciable diminution, even when the volume of the circulating fluid was seriously diminished. The vasomotor failure finally occurring should be regarded as the result and not the cause of the circulatory disturbances, and should, like the failure of respiration, be considered as a sign of approaching death. On the other hand, the decrease of the blood-volume begins in the earliest stage of peritonitis, and in the final stage this decrease is most conspicuous. There can be little doubt that the vasomotor centre tenaciously retains its activity almost until death. The decrease of the excitability of the vasomotor centre in the last stages of peritonitis probably depends on lack of circulating fluid and asphyxia of this centre. In two experiments the blood-pressure was raised by the injection of gum acacia, and a return of the response to stimulation of the peroneus nerve was observed. 'The most probable explanation of these experiments is that the vasomotor centre had lost its excitability because of the low blood-pressure, since it cannot well be assumed that injection of gum acacia would revive the centre were it really paralysed by the action of bacterial toxins.' In view of the striking similarity between secondary shock and peritonitis, it is probable that the reduction of the blood-volume is due in both to the same causes, i.e. dilatation and increased permeability of the capillaries with stagnation of blood in the dilated capillary areas, and filtration of plasma through the injured capillary walls.

The methods at present in general use in the treatment of the circulatory disturbances in peritonitis are of little or no value. As long as the blood-pressure is normal, vasoconstrictor drugs are useless, and when the blood-pressure falls appreciably the patient is moribund. Vasoconstrictor drugs may even be harmful, for a high blood-pressure is not indicative of an efficient circulation or an adequate supply of oxygen to the tissues. If, as is probably the case, the arteries in peritonitis are already constricted so as to compensate for the reduced blood-volume, a further vasoconstriction by adrenalin, for example, may cause a decrease of the amount of blood supplied to the tissues and asphyxia. The intravenous injection of saline solutions is of little value, as they leave the circulation very quickly. The continued infusion of several litres of normal saline solution, containing a small quantity of adrenalin, is recommended in Germany, but it is doubtful if even 4 litres given in this manner in 24 hours causes an increase of the blood-volume; the addition of adrenalin to saline solutions administered by intravenous injection greatly accelerates their elimination from the blood-stream. These bulky infusions may lead to severe oedema of the subcutaneous tissues and pulmonary complications. There remain the alternatives of transfusion of blood and the injection of solutions of gum acacia, which leave the blood-stream more slowly than do saline solutions. The latter may give rise to serious complications, and transfusion of blood is probably the best method of restoring the circulation in peritonitis.

C. L.

Moure, Paul. Traitement de la hernie ombilicale et de certaines éventrations par le cerclage de l'anneau au fil de bronze. [**Treatment of umbilical and other ventral hernias by closing the ring with a bronze wire.**] *J. de chir.*, 1922, **19**, 359-64.

Moure has had excellent results from this method. A large elliptical, transverse incision is made, the hernia separated and the contents reduced, excessive omentum being resected, if necessary. The sac, fascia, subcutaneous fatty tissue, and skin are excised *en masse*; then the cut peritoneal edges are raised and a purse-string suture of bronze wire is introduced, drawn tight, and tied. The superficial tissues are then sutured in layers in the ordinary manner. Moure claims that this method has the advantages of simplicity, rapidity, and solidity, and that it is especially of value in strangulated umbilical hernia. The bronze wire is well tolerated. He has done the operation ten times. C. C. C.

Schultz, P. J. Über männliche Genital- und Urogenitaltuberkulose. [B.] [**Genital and urogenital tuberculosis in the male.**] *Ztschr. f. Tuberk.*, 1922, **36**, 81.

Schultz has studied the 125 cases of genital and urogenital tuberculosis in the male found among 14,086 cases coming to necropsy between 1908 and 1920 at the Pathological Institute of the Berlin-Moabit Hospital. These 125 cases were invariably associated with tuberculosis elsewhere, chiefly in the lungs and pleurae. The organ in the urogenital system most often affected was the prostate, which was the seat of tuberculous changes in as many as 104 cases (83·2 per cent.). Tuberculosis of the vesicula seminalis was found in 78 cases (64·4 per cent.), and in the epididymis in 66 cases (52·8 per cent.). In as many as 35 cases the only constituent of the genital system affected was the prostate; in 12 of these cases tuberculosis of the urinary system was also found, and only in 23 cases was the disease in the prostate unaccompanied by tuberculosis elsewhere in the genital and urinary systems. These 23 cases were probably due to infection by the blood-stream. Previous to 1912 no case of isolated, 'genito-primary' tuberculosis of the epididymis had been found in the Berlin-Moabit Hospital, and since then only 4 or 5 such cases have been observed. Among the 65 cases in which the disease existed in the genital but not in the urinary system, there were as many as 48 with disease of the prostate. With regard to the direction of spread of tuberculosis in the genital system, Schultz discusses the claims of the 'testipetal' and 'testifugal' schools, and concludes that the prostate, in the overwhelming majority of cases, is the centre from which other parts of the genital system become infected. Were it not for this gland, which marks the junction of the genital with the urinary system, tuberculosis of the epididymis would be as infrequent an associate of renal tuberculosis in the male as tuberculosis of the Fallopian tubes is an associate of renal tuberculosis in the female. C. L.

DE QUERVAIN, F. Relationship between histological structure and biological activities of goitre tissue. *Surg. Gynec. & Obst.*, 1922, **34**, 513.

After reviewing briefly the work of investigators and the effect of thyroid extracts on tadpoles, and showing that tumours of the thyroid contain substances corresponding biologically to those in the normal gland, the author gives the results of further investigations by the same biological method, not only of goitrous tissue but of venous blood from the thyroid gland and from any other large vein of the systemic circulation. In these experiments rats were used and the effects of thyroid tissue estimated, for it has been shown by Streuli and Duran that rats when fed or injected with normal thyroid become hypersensitive to a deficiency of oxygen. Thyroidectomized rats bear rarefied air longer than healthy rats, and those treated with thyroid preparations bear it less long. A large series of experiments were carried out, and the results show that: (1) Feeding rats with goitrous substance always causes an increased sensitiveness to lack of oxygen. This was most marked with exophthalmic goitre containing a little colloid, and then in decreasing order with non-toxic colloid goitre, general parenchymatous enlargement, adenomatous goitres from non-cretins, and the same from cretins. (2) The injection of serum from thyroid veins produced in all cases a positive reaction, but less strong than in thyroid feeding. The order of succession was the same. Blood from the arm veins is distinctly active in cases of colloid goitre and parenchymatous enlargement, but not distinctly in adenomatous goitres, whether from cretins or non-cretins. In three out of four cases of dwarf cretins with thyroid atrophy the blood from the arm produced a decrease in the sensitiveness to lack of oxygen. A. J. W.

ROMANIS, W. H. C. The surgical treatment of exophthalmic goitre. *Lancet*, 1922, ii, 471.

Present surgical treatment is based upon the assumption that Graves's disease is due to a hyperthyroidism. It is probable that this hyperthyroidism is due to some cause which affects the other ductless glands. There is no sharp line of distinction between exophthalmic goitre and the other varieties of goitre. Statistics of Graves's disease should therefore only include typical cases. Ligature of the thyroid arteries is ineffective and may be described as the attempt of one who would like to, but dare not, remove part of the thyroid gland.

Until recently the mortality was exceedingly high, but in Romanis's series of 250 cases only six, or 2·4 per cent., have succumbed. He believes that this low mortality is largely due to the use of local anaesthesia, for of the six who died two were operated upon under ether. Of his cases only two have been refused operation on the ground that they were too advanced. Very early cases are given a course of medical treatment first. In severe cases medical treatment is very valuable as a preliminary to operation, but an operation should not be performed if the patient is very adverse to it. Mental symptoms of a maniacal, delusional, or melancholic type are a definite contra-indication, for an operation may make the condition worse. The other contra-indications are: an age over 65, the presence of diabetes or other gross constitutional disease, great fear or unwillingness to undergo operation, and the presence of oedema due to a failing heart.

In almost all of the author's cases the operation was performed under a local anaesthesia with a preliminary injection of morphia and hyoscine. If a permanent cure is aimed at it will be necessary to remove one lobe, the isthmus, and a third or even half of the other lobe. Hemithyroidectomy is hardy ever sufficient. It is usually feasible to remove the whole amount at one operation, but in very severe cases the excision may require to be carried out in two stages. In the performance of the operation the parathyroids may usually be ignored. In Romanis's series of cases a second operation has only been necessary in eight cases.

The after-treatment needs little comment. A fine tube is inserted for twenty-four hours. A long stay in bed and four months of very easy life are essential parts of the treatment. The results of the series may be summed up as follows: there is a mortality of 2·4 per cent. Of the remainder, after three or four months, the majority feel well, eat well, sleep well, and can do their day's work. The pulse-rate may, however, not come down to normal; the nervous excitability, tremor, and jumpiness are very much improved, but the exophthalmos, although much less marked, rarely if ever vanishes completely. (Many cases have, however, now been seen and published in which the exophthalmos has completely disappeared after operation.) The patients who receive surgical treatment comparatively early should, if a sufficient amount of thyroid tissue has been removed, become perfectly well. The advanced cases, with secondary changes in the heart, may never be absolutely cured. A. J. W.

Crile, G. W., and **Lower, W. E.** **The technique of operations on the thyroid gland.** *Surg. Gynec. & Obst.*, 1922, **34**, 258.

Ligation of vessels. This is always performed under local anaesthesia without removing the patient from bed. The superior artery is ligated in preference to the inferior, for it is more superficial and its ligation is apparently more effectual, probably because the nerve-supply of the gland runs with it. The whole field is infiltrated with 1 : 200 novocaine. The skin is incised in the line of its folds and the fascia is divided vertically. The muscles are not divided but the fibres separated. The artery is thereby exposed and ligatured. A second ligature is passed around all or most of the superior pole to make sure that the artery is included. The area is flooded with 1 : 600 quinine and urea hydrochloride and the skin incision closed with clips.

Typical resection. The skin and subcutaneous tissue are infiltrated with 1 : 200 novocaine and a collar incision made. The platysma is divided and reflected with the skin. The preglandular muscles are in the majority divided transversely, but if the goitre is small a vertical separation of the fibres suffices. The division is accomplished between muscle-clamps. The capsule and gland are now infiltrated with novocaine (this is especially important in exophthalmic goitre), the superior vessels are ligatured, and the gland resected. The whole of the anterior portion and the isthmus is removed, haemorrhage being prevented by first grasping the tissue with forceps. All vessels are ligatured. Preglandular muscles are sutured and the wound closed, a small drain being inserted into the centre.

A. J. W.

NEUROLOGY

Pette, H. Über diffuse Karzinose der weichen Hirn- und Rückenmarkshäute. [**Diffuse carcinomatosis of the lepto-meninges of the brain and spinal cord.**] *Deutsch. Ztschr. f. Nervenheilk.*, 1922, **74**, 226.

On pathological grounds, Pette differentiates two classes of diffuse malignant disease of the lepto-meninges, primary endothelial growths of the pia, and carcinomatous metastases. Clinically, the distinction cannot be made. He reports two cases. (1) An alcoholic male of 50 was admitted to hospital in a stuporose state, with a history of five epileptiform attacks during the preceding four weeks. The pupils were unequal, dilated, and almost inactive. The fundi were normal, but both vision and hearing were grossly diminished in acuity. All the reflexes were abolished. Head retraction rapidly developed and there was frequent vomiting. The cerebrospinal fluid was under great pressure and contained a few lymphocytes and some large epithelioid cells. The patient gradually sank and died six weeks after the sudden onset of symptoms. He became completely deaf and blind before death. At autopsy there was found a large tumour of the left parotid, which could not be examined or removed. The whole pia-arachnoid covering brain and cord was pale yellow in colour and opaque. It was of unequal thickness, and scattered over the inferior surface of the frontal lobes were numerous tiny nodules. At the vertex was a larger nodule 'of the size of a cherry'. Microscopical examination showed that the lepto-meninges were uniformly infiltrated by cells of epithelial character with scattered nodules of the same cells. At places they had tracked along small vessels into the brain substance, but there was no infiltration of the cord. The nerve-roots, both cranial and spinal, were similarly surrounded. The cerebral cortex was the seat of recent glial proliferation, and compound granular corpuscles and small round cells were present. The ganglion cells showed Nissl's acute degenerative changes.

The cellular character of the growth was that of a secondary carcinoma. Unfortunately, the parotid tumour could not be examined, but Pette suggests that it may have been a mixed tumour undergoing malignant degeneration.

(2) A man of 59 was taken acutely ill with headache, vertigo, vomiting, and pains in the chest. Examination revealed slight right-sided hemiparesis with increased tendon-reflexes on that side. The fundi was normal, but both vision and hearing were markedly diminished in acuity. The cerebrospinal fluid was under pressure and contained a few lymphocytes and some large epithelial cells. Epileptiform seizures and head-retraction occurred as in the previous case, and death ensued after four weeks' illness. Autopsy revealed a carcinoma of the pylorus. The lepto-meninges, beyond appearing a little thickened and opaque, seemed normal on naked-eye examination. Microscopic examination revealed a condition identical with that found in the first reported case, but less uniformly diffused. The cellular character of the growth was similar, and the cells found in the cerebrospinal fluid proved to be like those in the meninges.

Pette believes that both blood-vessels and lymphatics (including perineural lymphatics in the region of the primary growth) act as channels of dissemination, and an important immediate channel may be the cortical blood-vessels. The commonest seat of the primary growth in reported cases of the kind seems to be the stomach.

The clinical picture is characteristic and resembles that of an acute cerebrospinal meningitis. The illness opens with headache, vertigo, vomiting, and mental obfuscation. Signs of generalized meningeal irritation follow, with epileptiform attacks and head-retraction. The cranial nerves are affected, leading to pupillary changes, deafness, and blindness. Spinal nerve involvement appears as arreflexia and root pains. The course of the illness is rapid and fatal. The presence of tumour-cells in the cerebrospinal fluid is diagnostic.

In the discussion which followed the reading of this paper at a meeting of the Society of German Neurologists, Rindfleisch observed that there was also a diffuse sarcomatosis of the lepto-meninges. The clinical picture was one of meningitis with fever, and the cerebrospinal fluid showed inflammatory characters and contained tumour-cells. F. M. R. W.

Siemerling, E., u. **Oloff, H.** Pseudosclerose (Westphal-Strümpell) mit Cornealring (Kayser-Fleischer) und doppelseitiger Scheinkatarakt, die nur bei seitlicher Beleuchtung sichtbar ist und die der nach Verletzung durch Kupfersplitter entstehenden Katarakt ähnlich ist. [**Pseudosclerosis with corneal pigmentation and a haze on the lens visible only on oblique illumination, and resembling a condition produced by the presence of copper in the eye after perforating injuries.**] *Klin. Wchnschr.*, 1922, **1**, 1087.

The authors describe the case of a man of 43, employed in a brewery and in the habit of drinking daily 4 litres of beer and of smoking excessively, who, for six years before the examination now reported, had gradually developed tremor of the head and limbs. At the end of this period he presented a Parkinsonian facies and widespread tremor. This was minimal when he lay down, but became coarse and forceful during movement. Its rhythm was two per second. The musculature was markedly hypotonic, the tendon-jerks normal, the abdominal reflexes absent, but the state of the plantar responses is not mentioned. Articulation was slow, but otherwise normal. Cerebration was normal. The Wassermann reaction was negative in blood and cerebrospinal fluid, but the latter showed an increased globulin content and 17 lymphocytes to the cubic mm. The liver was definitely enlarged and its edge was palpable four fingers' breadth below the costal margin. The spleen was not enlarged. Hepatic tests gave no definite indication of defective liver function, beyond a very slight levulosuria. Examination of the eyes showed the presence of the characteristic green-brown pigment ring at the periphery of the cornea, and also a blue-grey haze on the surface of the lens resembling a sunflower in outline. This was visible only on oblique illumination. The authors point out that the lens condition exactly accords with that described some years ago by Purtscher as indicating the presence of minute fragments of copper in the eye in cases of perforating injury, and occurring apart from the presence of copper in the lens itself. Since this haze differed from all other forms of lenticular opacity in being invisible by transmitted light—that is, on ophthalmoscopic examination—Purtscher spoke of it as a 'Scheinkatarakt', or 'apparent cataract'. The authors regard this new observation as tending to confirm the toxic-infective origin of the pseudosclerosis-progressive lenticular degeneration group of cases, to which they believe their case to belong. They accept the view originally formulated by Kinnier Wilson, and erroneously attributed by them to German writers, that a poison formed in the diseased liver acts upon the nervous system, producing a selective lesion in the corpus striatum. They find in Spatz's observation (cf. *Medical Science*, 1922, **6**, 493) that the globus pallidus and substantia nigra contain an excess of iron pigment, an indication of a special biochemistry in these structures which might under the conditious of disease lead to selective destruction of them. Apparently certain structures in the eye would be similarly affected, as the present case indicates. Unfortunately, the authors have voluntarily restricted the scope of their discussion on the subject by confining their attention to German writings exclusively. F. M. R. W.

Gerson, M. Zur Ätiologie der multiplen Sclerose. [**On the aetiology of multiple sclerosis.**] *Deutsch. Ztschr. f. Nervenheilk.*, 1922, **74**, 251.

Gerson has examined the condition of the tonsils and of the mucosa of the nasopharynx in eleven cases diagnosed as multiple sclerosis. In all of these he found lesions of the nasopharyngeal mucosa, and in ten of them pathological changes in the tonsils. The mucous lesions are described as including hypertrophic and atrophic rhinitis. The tonsils were either enlarged or atrophic and indurated, and in both instances contained pus. He suggests that the tonsils may be the port of entry of the virus responsible for the disease. He outlines the following course of events; chronic infection of the tonsils, perineural lymphatic spread up the sensory nerve filaments surrounding the tonsils to the central nervous system, and a secondary trophic lesion in the mucosa of the nasopharynx. Intercurrent diseases or trauma may be the immediately determining factors in an invasion of the nervous system along this channel. He also thinks it possible that occasionally other primary sites of infection may be productive of multiple sclerosis by the same process. Six cases of the series were subjected to operative procedures on the tonsils and nasopharynx to clear away the source of infection. In each of these a transient initial increase of nervous symptoms was followed by pronounced betterment. F. M. R. W.

Auerbach, S. Über zentrales Fieber nach Gehirn- und Rückenmarksoperationen. [**Fever of central origin after operations on the brain and spinal cord.**] *Deutsch. Ztschr. f. Nervenheilk.*, 1922, **74**, 239.

Auerbach deals with this subject in a short paper read before the eleventh annual meeting of the Society of German Neurologists at Brunswick in 1921. He quotes two cases of prolonged fever, without evidence of infection, after operations on the central nervous system. The first was that of a girl from whom a fibrosarcoma compressing the entire cervical enlargement of the cord was removed. There was considerable loss of cerebrospinal fluid, which continued to leak for twelve days. This was the duration of the fever, which cleared up as soon as the wound closed. The second case was that of a boy of 3¾ years, from whose cerebellum a small glioma was removed. Fever persisted for nine days, though there was no escape of cerebrospinal fluid. Autopsy revealed no signs of infection. Reviewing the surgical literature, he finds that Krause alone has referred to the subject. Krause believes that the operative handling and compression of the brain by spatulas is an adequate cause in some cases, and that in others, including spinal cases, pressure of cerebrospinal fluid, or the loss of large quantities of the fluid, is responsible. No details are given as to the possible mechanism at work in producing pyrexia in these circumstances. Turning to diseases of the central nervous system, Auerbach finds that tumours in the region of the basal ganglia and epidemic encephalitis are most commonly associated with fever, which accords with the physiologists' localization of heat-regulating centres in this region. Jacoby and Römer have suggested that distension of the ventricles by cerebrospinal fluid, or circumstances giving rise to 'irritation' of the ventricular walls may be the cause of pyrexia. Various other speculations are also briefly mentioned.

F. M. R. W.

Burr, C. W. Heredity in epilepsy: a study of one thousand four hundred and forty-nine cases. *Arch. Neurol. & Psychiat.*, 1922, **7**, 721.

The author confines his remarks to cases of what is called 'idiopathic epilepsy'. He finds no less than 621 cases of serious nervous and mental disease in the relatives of the 1,449 cases of epilepsy studied. Direct inheritance does not appear to be important, since the parents were epileptic in 34 instances only. On the other hand, the frequency of insanity, chorea, alcoholism, crime, and epilepsy in relatives of patients points to congenital instability resulting from abnormality of the germ-cell. 'Considering all the data, it is safe to assume that the effect of heredity is rarely direct, that usually it is indirect and general, not specific. In other words, a predisposition to nervous or mental disease is inherited; the resulting specific disease depends upon external causes . . .' In considering the organ or organs at fault in epilepsy, he believes that the ductless gland and psychogenetic schools of thought are less likely to solve the riddle than the biochemist.

F. M. R. W.

Reports of the Salvarsan Committee. II. Toxic effects following the employment of arsenobenzol preparations. *Medical Research Council, Special Report Series*, No. 66, 1922.

Contained in this valuable report is much information of special interest to neurologists. The committee finds that no special arsenobenzol preparation can be regarded as more likely than others to produce ill effects, and that errors in technique cannot account for more than a few accidents. The most important ill effects which may end fatally are: encephalitis haemorrhagica, acute yellow atrophy of the liver, and exfoliative dermatitis and its complications. Of these, the first named appears to have been the most frequently observed in Germany, while in England and America the second and third are more frequently recorded. *Encephalitis haemorrhagica.* About half the total recorded 'salvarsan deaths' have been due to encephalitis. The symptoms appear from two to five days after injection and, for the most part, end fatally within twenty-four to forty-eight hours. It is believed to be commonest during the secondary stage of syphilis (that is, when most cases come under treatment), and its occurrence does not appear to be related to the particular compound used. The majority of cases occur after the second injection. The illness is ushered in by intense headache, shivering, vomiting, and sometimes by fever. On the following day the patient suddenly has an epileptiform convulsion with clonic spasms, followed by unconsciousness. The tendon reflexes are abolished, there is an extensor plantar response, and ocular palsies and other signs of central nervous involvement appear. Coma with intercurrent epileptiform convulsions continue until death. There is commonly retention of urine. Two views have been expressed as to the origin of this condition: that it is an acute cerebral syphilis of the nature of an 'Herxheimer reaction': that it is a direct result of salvarsan, probably in susceptible persons. The bulk of evidence supports the latter view. Marschàlko and Veszprèmi appear to have given the most complete account of the morbid anatomy of the condition. Macroscopically, haemorrhages were observed in different parts of the brain, sometimes punctiform and sometimes larger when small haemorrhages were aggregated. These were most thickly scattered in the pons. No gross areas of softening were observed. Microscopically, minute capillary thromboses and haemorrhages were the characteristic lesions. A few cases are recorded of encephalitic symptoms with recovery. As to treatment, the committee suggests bleeding up to 18 to 20 oz., the withdrawal of 15 c.cm. of cerebrospinal fluid by lumbar puncture, and intramuscular injection of 1·5 c.cm. of 1 in 1,000 adrenalin. All these measures should be carried out as early as possible after the onset of symptoms. A somewhat rarer complication of arsenobenzol treatment is *polyneuritis.* Commonly it follows the development of dermatitis, but has been known to precede it. In some cases, it appears about seven weeks after the cessation of treatment, when this has been rendered necessary by the appearance of dermatitis. From the descriptions given the polyneuritis appears to have nothing specific in character, and resembles polyneuritis from other causes, with the addition of the skin changes seen in arsenical neuritis. F. M. R. W.

Porges, O., u. **Adlersberg, D.** Über neurotische Atmungstetanie und über die Behandlung der Tetanie mit Ammonphosphat. [**Tetany of respiratory origin occurring in hysteria, and the treatment of tetany with ammonium phosphate.**] *Klin. Wchnschr.*, 1922, **24**, 1200.

The authors refer to the papers on tetany, which have recently been abstracted in this Journal (1922, **6**, 388), and with which they agree. Studies made before the war by the authors indicated that over-ventilation is not of rare occurrence in hysteria, and may be associated with symptoms of tetany. They briefly describe two personally observed cases of the kind occurring in hysterics as a result of physical and psychical trauma. A second group of cases is that in which attacks of excessive breathing followed by the appearance of tetany occur as isolated hysterical manifestations, sometimes of great frequency. While Haldane and his followers regard an anoxaemia, produced as previously described here (1921, **4**, 427), as the direct cause of the tetany, Porges and Adlersberg, following Grant and Goldman, believe an alkalosis to be responsible. This leads to a diminished solubility of the calcium salts in the blood, which is the direct cause of the symptoms. Recently, Freudenberg and György have described tetany in infants following the administration of ammonium chloride, a salt known to produce acidosis. The present authors have accordingly produced an acidosis by one or other of the following methods: the use of a carbohydrate-free diet, the breathing of air containing excess of CO_2, muscular exertion leading to CO_2 production, and the administration of ammonium salts. Acidosis produced by any of these methods may be accompanied by symptoms of tetany. Practically, the most useful method is the administration of ammonium phosphate, though repeated doses may lead to diarrhoea. Acidosis develops on the second day and persists for about two days. Simultaneously, symptoms of tetany appear. The observation is of interest in view of what has been called 'phosphate tetany', a form produced by the administration of phosphates (Bing, Elias, Jeppsson).

F. M. R. W.

ADRIAN, E. D., and **FORBES, A.** **The all-or-none response of sensory nerve-fibres.** *J. Physiol.*, 1922, **56**, 301.

In observations previously reported (cf. *Medical Science*, 1920, **1**, 628), Adrian found that there was no evidence of two systems of afferent sensory nerves, such as had been suggested by Head on clinical and by Ranson on histological grounds. The present paper records the results of an investigation of the nature of the nervous impulse in sensory nerve-fibres. The authors find that the response of a sensory nerve-trunk (as determined by the reflex motor effect) to a single, momentary stimulus may vary in two ways: (*a*) a strong stimulus will excite more fibres than a weak stimulus; and (*b*) a stimulus which is more than strong enough to excite all the fibres may set up two or more impulses in each fibre. The gradation of reflex motor response appears to depend upon the number of nerve-fibres stimulated and the repeated excitation by strong stimuli. In general the reactions of the reflex arc support the view that the large majority of sensory fibres react according to the all-or-nothing principle.

F. M. R. W.

BARRINGTON, F. J. F. **The nervous control of the urinary bladder in amphibians.** *Brain*, 1922, **45**, 126.

These observations amplify Barrington's earlier work on the nervous control of micturition, which has been described by the author himself in a previous number of *Medical Science* (1921, **5**, 220). Their purpose was to determine whether, as is the case in the cat, the normal evacuation of the bladder demands the integrity of some part of the anterior (cephalad) part of the hindbrain. The animals used were frogs, toads, newts, and salamanders. They were anaesthetized by immersion in ether water, the skull opened, and the brain-stem transected at the desired plane. They were then kept under observation for two days. When killed, the animals fell distinctly into two groups according to the state of the urinary bladder. In one group this organ, and the abdomen secondarily, were tensely distended, in the other, the bladder, although containing urine, showed a crenated wall. Transections cephalad to the posterior part of the midbrain did not result in distension, and it was necessary to remove the posterior (caudad) part of the midbrain to produce distension. This localization corresponds to that found in the cat. Although, in such small animals as those under observation, exact details are difficult to obtain, it seems probable that in them, as in the cat, the distension is due to paralysis of the bladder-wall, the expulsive mechanism, and not to tonic contraction of the sphincters.

In frogs and toads the spinal cord was divided at various levels from the second to the fifth roots. Great distension of the bladder resulted. Division of the cord caudad to the seventh roots did not result in distension of the bladder. As in the case of the mammal, two sets of nerves supply the bladder in the frog. These pass out of the cord in the seventh, ninth, and tenth roots respectively. Division of either set singly, that is, seventh, or ninth and tenth, does not result in distension of the bladder, to produce which it is necessary to divide both sets bilaterally. Comparable results were obtained in the urodela (newts and salamanders), although in the case of the latter animal there was no evidence of two sets of efferent nerves to the bladder.

It follows, therefore, that in amphibians, as in mammals, the integrity of a brain-stem centre, situated in the region of the caudad end of the midbrain is necessary for normal evacuation of the bladder. F. M. R. W.

Langley, J. N. The nerve-fibre constitution of peripheral nerves and of nerve-roots. *J. Physiol.*, 1922, **56**, 382.

Ranson believes (cf. *Medical Science*, 1920, **1**, 628) that in spinal nerves and in their posterior roots numerous small non-myelinated fibres exist and outnumber the myelinated fibres. Langley has investigated this and several other points in connexion with the constitution of peripheral nerves. He finds that cutaneous nerves contain many non-myelinated fibres, the nerves to skeletal muscle few. This result does not favour the view that these fibres have any considerable connexion with striated muscle. Very few, probably no, non-myelinated fibres enter the spinal cord by the posterior roots. All anterior roots are distinguished from posterior roots by their containing a relatively large proportion of fibres 13μ and more in diameter, and a relatively small number of fibres of about $7{\cdot}5$ to 11μ. The various rootlets of a nerve vary widely in their content of small fibres. In the posterior roots of nerves, which do not contain autonomic fibres in their anterior roots, there are a considerable number of fibres of 5μ, with a less number of 3μ. When the anterior roots contain autonomic fibres, the posterior roots corresponding have a greater number of 3μ, but not of 5μ fibres. The 3μ fibres in the posterior roots are probably afferents from unstriated muscle and glands. A large factor in determining the size of nerve-fibres is the nature of the tissue with which they may be connected. The material examined was obtained from cats. F. M. R. W.

Weigeldt, W. Elektromyographische Untersuchungen über den Muskeltonus. [**Electromyographic studies of muscle-tone.**] *Deutsch. Ztschr. f. Nervenheilk.*, 1922, **74**, 129.

As a result of electromyographic studies of various abnormal states of muscle-tone in cases of nervous disease, Weigeldt comes to the following conclusions. A differentiation of muscle-tone into distinct forms is not possible by this means. Neither clinically nor electrographically can tone be considered as a simple phenomenon. All degrees of muscular hypertonus may occur without the presence of any action current whatever. This applies to the rigidity of both pyramidal and extra-pyramidal diseases.

The author employed non-polarizable electrodes applied to the skin. These results differ fundamentally from those recorded by Rehn (cf. *Medical Science*, 1922, **6**, 392), and it is clear that little exact knowledge on electromyography exists. F. M. R. W.

PATHOLOGY

Bacot, A., and Ségal, J. The infection of lice (*Pediculus humanus*) with *Rickettsia prowazeki* by the injection *per rectum* of the blood-platelets of typhus-infected guinea-pigs and the reinfection of other guinea-pigs from these lice. *Brit. J. Exper. Pathol.*, 1922, **3**, 125.

The injection of lice (*Pediculus humanus*) with a concentrated emulsion of platelets obtained by fractional centrifugalizations of the blood of a typhus-infected guinea-pig affords a sure and quick method of obtaining the development of *Rickettsia prowazeki* in these insects. The lice thus infected can be used to convey typhus fever to fresh guinea-pigs. The parallel development of typhus virus and *Rickettsia prowazeki* in successively passaged guinea-pigs is demonstrated, and also in lice infected from guinea-pigs after 23 blood or brain passages. P. F.

Warthin, A. S. The occurrence of *Entamoeba histolytica* with tissue lesions in the testis and epididymis in chronic dysentery. *J. Infect. Dis.*, 1922, **30**, 559.

The case is reported of a Russian Jew, the subject of recurrent attacks of amoebic dysentery for eleven years. Symptoms having pointed to abscess of the liver, a laparotomy was performed with a negative result. Death ensued five days later from pneumonia. The lesions at autopsy are described, the most interesting being the metastases of *Entamoeba histolytica* in the epididymis and testis of both sides. The amoebic dysenteric lesions were found nearly healed. In the lesions in the rete testis and efferent tubules there were blood-clots with entamoebae. In the dilated parts of the epididymis they were also found with spermatozoa in their interior. The lesions in the genital organs are stated to be unique.
W. B.

Harris, D. T. Active hyperaemia. *Proc. Roy. Soc.*, 1922, B. **93**, 384.

The author first reviews the existing knowledge of vasoconstrictor nerves (neuroparalytic hyperaemia), of vasodilator nerves (neurotonic hyperaemia), of vasodilator substances (producing a local hyperaemia), and of functional hyperaemia. The object of this investigation is stated by the author to be:

(1) To obtain evidence, if possible, for the undoubted existence of vasodilator nerves.

(2) To determine the relative part played by metabolites and vasodilator nerves in functional hyperaemia.

(3) If vasodilator nerves exist, and are not an essential to functional hyperaemia, what is their function?

Then follow details of the methods used to investigate the above points. Vasodilation is measured by directly determining the venous outflow as shown by a drop recorder. Also an indirect determination was made by a plethysmograph of the tongue. The theory which explains vasodilation by the action of metabolites was examined experimentally. Estimations were made of the alkali reserve of the blood from the lingual vein and femoral artery during stimulation of the lingual nerve, and shown to be practically identical. Furthermore, no real difference was detected in the lactic acid content of the blood issuing from the tongue during stimulation of the lingual nerve as compared with that in the femoral artery. It was concluded that the lingual nerve contains true vasodilator fibres just as the sympathetic contains vasoconstrictor fibres. Both are equally independent of the intervention of metabolites.

No evidence was found that functional hyperaemia is due either to diminution in vasoconstrictor tone or to increase in vasodilator tone. The experiments show that the increased blood-supply during muscular activity is due entirely to the products of metabolism. The absence of a simultaneous excitation of the vasodilator nerves during voluntary movement, though probable, is not proved. Of the metabolites investigated CO_2 and α OH organic acids were found to be increased.

Apart from muscular activity, one function of vasodilator nerves was found to be concerned with the control of body temperature. Active hyperaemia in the dog's tongue may be induced by reflex excitation of the vasodilator nerves through stimulation of heat receptors in the skin.

Whether the vasodilator of the tongue plays any part in the sensation of taste was not investigated. W. A. M. S.

Ebeling, A. H. A ten-year-old strain of fibroblasts. *J. Exper. M.*, 1922, **35**, 755.

A short, but interesting, communication giving an account of a strain of fibroblasts which has been cultivated for 10 complete years and is now in the 1,860th generation. The strain was originally isolated from the heart of a chick embryo on January 17, 1912. To-day the growth is as rapid as before, and it is now demonstrated that tissue-cells living *in vitro* transform the foodstuffs of their medium into protoplasm, and that their mass increases. The existence of the ten-year-old strain demonstrates also that the cells are potentially immortal. W. B.

Cramer, W., Drew, A. H., and **Mottram, J. C. On blood-platelets; their behaviour in 'vitamin A' deficiency and after 'radiation', and their relation to bacterial infections.** *Proc. Roy. Soc.*, 1922, B. **93**, 449.

The authors found that the absence of fat-soluble vitamin from the diet always leads, in the rat, to a progressive diminution of blood-platelets, and they regard the thrombopenia as the lesion characteristic of this deficiency, just as lymphopenia, in their opinion, is characteristic of vitamin B deficiency. Thrombopenia may be found in rats kept upon a vitamin A-free diet, even although, to all appearances, they are normal. When profound thrombopenia has been established, addition of the missing vitamin A to the diet is followed by a rapid increase in the number of platelets up to the normal, provided that the animal has not been allowed to suffer too long and too severely from deficiency. Exposure to radium produces not only lymphopenia, but also, with sufficiently large doses, thrombopenia. From this the animals recover rapidly, provided that the application of radium is discontinued and that the dose has not been excessive. If by exposure to radium or by witholding the fat-soluble vitamin the number of platelets has been reduced below a certain critical level (about 300,000 for the rat), the resistance of the animal to infection is greatly diminished and infections develop spontaneously. If the platelets increase the infections may clear up. Blood-platelets fulfil an important function in the mechanism of resistance to bacterial infection. Alterations in local or general resistance to infection are associated with local or general conditions in distribution of platelets. W. B.

Torraca, L. L'influenza dell' irradiazione solare sul processo di guarigione delle ferite studiata in montagna. [**Influence of solar radiations on the healing of wounds investigated at high altitudes.**] *Gior. d. r. Accad. med. di Torino*, 1922, **84**, 412.

Experimental investigations. Sunlight has a beneficial influence on the healing of wounds. This beneficial effect is greater if the rapid cooling of the wounds, after exhibition to solar radiations, is prevented by means of a bandage. C. D. F.

Omodei-Zorini, A. Contributo sperimentale allo studio della metaplasia mieloide della milza. [**Experimental contribution to the study of myeloid metaplasia of spleen.**] *Pathologica*, 1922, **14**, 257.

Experiments were made by means of rabbits and guinea-pigs, which were repeatedly injected with mixtures consisting of four-fifths of blood-serum and one-fifth of fluid obtained by pressing the blood-clot between two pieces of sterile gauze. The mixture thus prepared contained, besides normal serum, small quantities of fibrinogen and haemoglobin, as well as some blood corpuscles. The results obtained varied according to the nature of the mixture. When this was formed of heterogeneous serum and fluid, the haemolytic activity of the spleen and the myelogenetic and erythrogenetic function of the bone marrow were particularly excited. When the mixture was homogeneous with the animal experimented upon, the haematopoietic function of the spleen was awakened, as shown by the presence in its pulp of many foci of myeloid metaplasia. According to the author, this last result should be connected with the presence in the mixture of red blood corpuscles from the same species as that of the animals used for the experiment. C. D. F.

Melchior, L. Om Sektionsfund og Dödsaarsager hos Patienter med erhvervet Syfilis. [**Necropsy findings and the causes of death in patients with acquired syphilis.**] *Hosp.-Tid.*, 1922, **65**, 106–8.

Among 4,717 persons over the age of 15, examined *post mortem* by Melchior between 1914 and 1920, there were 358 (7·6 per cent.) with a history of, or clinical or post-mortem signs of, syphilis. The proportion of men to women was as 69 to 31. The age at death differed considerably from that of all the cases, 65·4 per cent. of the syphilitic having died between the ages 30 and 60, whereas only 46 per cent. of all the persons examined *post mortem* had died within these ages. Only 25·1 per cent. of the syphilitic had died after the age of 60, and only 7·2 per cent. after the age of 70. A history of infection was obtained in 54 per cent., and the date at which infection had occurred was ascertained in barely 50 per cent. About half the number of the patients in the latter class were found to have died within 5 to 25 years of infection, and 15 per cent. had died within 3 years of infection. But among these early deaths there were doubtless several due to causes other than syphilis. Clinical signs of syphilis (Wassermann not included) during the patient's last residence in hospital were demonstrable in about 26 per cent. (93). In 28 of these cases the skin and mucous membranes were involved, in 10 the bones and joints, in 10 the aorta, and in 54 the central nervous system.

Comparing his observations with those of Grön's in 1897, Melchior finds that tertiary lesions of the skin and bones have become much more rare. In 159 cases (44·4 per cent.) there was a Wassermann record which in 102 cases was positive and in 57 was negative. Among the 102 positive Wassermann cases there were 84 showing signs of syphilis *post mortem.* Among the 57 negative Wassermann cases there were 31 showing signs of syphilis *post mortem.* Of the 115 persons showing residual signs of syphilis *post mortem,* 84 gave a positive, and 31 a negative Wassermann. Of 44 showing no residual signs of syphilis *post mortem,* 18 gave a positive and 26 a negative Wassermann. In 248 cases (69·3 per cent.) the necropsy showed signs of syphilis, and the frequency with which they were found *post mortem* increased steadily with the age of the patient. Thus, of syphilitic patients dying under the age of 30, only 23·5 per cent. showed signs of syphilis *post mortem,* whereas 88·5 per cent. of the syphilitic dying after the age of 70 showed such signs. Of the 248 showing signs of syphilis *post mortem,* 189 suffered from aortitis, 76 from disease of the central nervous system, 22 from disease of the liver, 19 from disease of the testicles, 9 from disease of the bones, and 14 from disease of the skin and mucous membranes. Unilateral renal atrophy was found in 5 cases, and lesions (amyloid disease not included) of other organs in 9 cases. Death was due to syphilis in 140 cases, disease of the aorta accounting for 82 deaths, of the central nervous system for 33 deaths, of the liver for 5 deaths. There were also 50 deaths which might have been due to syphilis, the morbid changes being profound anaemia, arteriosclerosis, haemorrhage and softening of the brain, myofibrosis of the heart, and chronic non-tuberculous pneumonia. In this category there were 20 cases of renal disease. In 162 cases syphilis could not be associated with the cause of death. C. L.

Rasch, C. Om Sektionsfund og Dödsaarsager hos Patienter med erhvervet Syphilis. [**Necropsy findings and the cause of death in patients with acquired syphilis.**] *Hosp.-Tid.*, 1922, **65**, 108–11.

Melchior's paper has drawn from C. Rasch a hitherto unpublished account of observations made 26 to 30 years earlier at the same hospital as that in which Melchior's investigations were made. In 1892 and for the next five years, Rasch sought for signs of syphilis in 3,000 adults coming to necropsy. In 204, or 7 per cent., there was either clinical or post-mortem evidence of syphilis, the proportion of men to women being 142 to 62. Clinical evidence of syphilis was obtained in 95 cases, and in 70 cases (34 per cent.) syphilis was the main cause of death. In 19 cases with clinical evidence of syphilis the necropsy showed no sign of it. Of the 70 cases in which syphilis was the cause of death, dementia paretica was responsible for 8, and various other diseases of the brain for 22. Myelitis and tabes were responsible for 5, aneurysm of the aorta for 9, amyloid degeneration for 5, syphilis of the liver for 3, heart disease for 3, pulmonary disease for 6, and renal disease for 9. In as many as 27 cases pulmonary tuberculosis was the dominant cause of death. Discussing his material, Rasch comments on the frequency with which he found chronic, indurative, fibrous pneumonia, with single or multiple bronchiectatic cavities, and often with fibrous pleurisies of remarkable thickness and density. As this condition was associated with signs of syphilis elsewhere, and there was no evidence of tuberculosis, Rasch is inclined not only to believe in the existence (doubted by many) of fibroid syphilis of the lung, but also to regard it as fairly common. He also regards unilateral or asymmetrical atrophy of the kidneys (observed in 17 of his cases) as a reliable sign of syphilis. C. L.

Kestner, O. Klimatotherapie im Krankenhaus. [**Climato-therapy in the hospital.**] *Beitr. z. Klin. d. Tuberk.*, 1922, **50**, 121–8.

Kestner has experimented, at the Physiological Institute in Hamburg, with dogs to test the action of the arc lamp on the blood. He quotes the observations made in 1912 by Laquer and Weber, who found that the rate of regeneration of blood in animals, artificially rendered anaemic, was much quicker and more complete at high altitudes than at low levels. Kestner has found that the rate of this regeneration is appreciably hastened by keeping the experimental animal in front of an arc lamp, whereas keeping it under a lowered atmospheric pressure has no such effect. He has also made dogs breathe air on which the arc lamp has acted, but has not exposed them directly to its rays. He found that the results were the same as when the dogs were exposed directly to the arc lamp, and he concludes that air, treated by the arc lamp, must contain a substance or substances, ozone perhaps, not present beforehand. With regard to the common observation that insolation and exposure to the arc lamp lower the blood-pressure appreciably, he points out that the explanation of this phenomenon has hitherto been that, the temperature of the body being raised, the cutaneous vessels are dilated, with a resulting fall in the general blood-pressure. He is sceptical about this view, for he has found that when patients and animals breathe arc lamp-treated air, but are not themselves exposed to the arc lamp, their blood-pressure falls considerably. But the blood-pressure falls little or not at all on exposure to the arc lamp when pure air, which has not been acted on by the arc lamp, is breathed. These observations have suggested the possibility of separating the principal effects of the arc lamp, so that its action on the blood-pressure can be reserved for cases in which lowering of the blood-pressure is desirable. In the past many patients have had to discontinue arc lamp treatment on account of an alarming fall of blood-pressure; in the future this complication may be avoided by exposing the patient to the direct action of the arc lamp, and letting him breathe pure air unaltered by the lamp. He should thus obtain the benefits of direct insolation without its deleterious effects. C. L.

BACTERIOLOGY

Skarić, J. Ueber die Beziehungen des *Bac. melitensis* (Bruce) zum *Bac. abortus infect. bovum* (Bang). [**On the relationship between *B. melitensis* (Bruce) and *B. abortus* (Bang).** *Ztschr. f. Hyg. u. Infektionskrankh.*, 1922, **95**, 358.

The author confirms the close relationship between *M. melitensis* and *B. abortus* which has been emphasized particularly by American writers. The action of *B. abortus* in man is still unsettled and the author thinks that it is not likely to be pathogenic. He cites the case of certain districts in Lower Austria in which cattle abortion was common although there were no reports of any possible action in human beings. The serum of human beings who had drunk the milk of cows suffering from abortion agglutinated *M. melitensis*. W. B.

Heist, G. D., Solis-Cohen, S., and **Solis-Cohen, M. A study of the virulence of meningococci for man and of human susceptibility to meningococcic infection.** *J. Immunol.*, 1922, **7**, 1.

The writers had previously described a test that had been applied to the demonstration *in vitro* of the relative susceptibility of animals to various infections. In this test, ‘ whole ’ coagulable blood as it issues from a blood-vessel was brought in contact with small numbers of bacteria adhering to the inner wall of capillary glass tubes. The bacteria and blood were incubated for 24 hours, being then examined microscopically to see whether or not the bacteria had developed. The present paper deals chiefly with this test as applied to meningococci. When these micro-organisms freshly isolated from the C. S. F. of cases suffering from meningitis are cultured in capillary tubes of ‘ whole ’ coagulable blood of normal men they grow rapidly. This ability, however, is not possessed by the majority of strains of meningococci recently isolated from the throats of carriers. It appears that spinal fluid strains are much more virulent than carrier strains, although among the latter there are degrees of variability. The ‘ whole ’ coagulable blood of most normal men permits the rapid growth of spinal-fluid strains of meningococci, a fact which, according to the authors, indicates that they are susceptible to attacks of meningococci that have passed into the nervous system. The blood of only one among many normal men permitted the growth of carrier strains, and it is probably in this group that cases of meningitis may be expected to occur from exposure to a carrier. This seems to be borne out by the fact that the unique case referred to was one of the authors (G. D. Heist), who fell a victim to cerebrospinal meningitis in 1920. His history is detailed in the paper. W. B.

Erickson, Mary, J., and Albert, H. Cultivation of the gonococcus. *J. Infect. Dis.*, 1922, **30**, 268.

The authors have made a comparative study of the value of ascitic agar, blood agar, serum agar, starch agar, blood serum, testicular agar, and oleate-haemoglobin agar as media for the growth of the gonococcus. They found testicular blood agar with a P_H 7·4 to 7·8 to be the most favourable medium both for isolation and subsequent cultivation. A proper reaction and moisture content and an absence of sodium chloride were found to be very important. Fermentation tests made with solid media containing 0·5 per cent. glucose with phenol red as an indicator showed a primary acidity followed by alkalinity. Contrary to recent assertions, reduced oxygen tension was found of no practical value either in isolation or subsequent cultivation. Studies on the effect of aniline dyes on the growth of the gonococcus and contaminating microbes were also made. Dyes of the violet and green series tended to inhibit staphylococci more than gonococci. Methyl violet added to blood testicular agar in a proportion of 1 : 200,000 to 1 : 500,000 was found to be of service in the isolation of gonococci in contaminated exudates. W. B.

Kelley, Margaret F. The precipitin reaction in the determination of the infectivity of gonorrheal discharges. *J. Infect. Dis.*, 1922, **30**, 623.

The authoress has tested the statement of Robinson and Meader (1920) that extracts of discharges from gonorrhoeal inflammations give precipitin reactions with antigonococcus serum even when smears from such discharges fail to show gonococci. It was found that although reactions occurred with extracts of gonorrhoeal discharges in the presence of antigonococcus serum from rabbits, similar reactions were also obtained with normal rabbit serum. Likewise extracts from non-gonorrhoeal discharges gave reactions with normal and immune sera. The authoress concludes that the precipitin reaction as recommended by Robinson and Meader is not applicable for the determination of the presence of gonococcus in discharges from the cervix and urethra. W. B.

Branham, Sara, E. The production of lung haemorrhages and associated phenomena in rabbits and guinea-pigs. *J. Infect. Dis.*, 1922, **30**, 670.

The authoress experimented with 32 rabbits and guinea-pigs, which received intratracheal inoculations with salt solution and filtered saline nasal washings from normal persons as well as from those suffering from colds. Sixteen of these animals were killed and the lungs of eight (50 per cent.) showed marked pulmonary haemorrhages and emphysema. Similar lesions occurred with equal frequency in normal uninoculated animals and in those inoculated intratracheally—a fact clearly demonstrated by Maitland, Cowan, and Detweiler (*Medical Science*, 1921, **4**, 154). These lesions were found only in animals killed by a blow on the back of the neck. In fact, 67 per cent. of all the animals killed by a blow exhibited the lesions, and the percentage rose to 87 when the blow was inflicted with the head held up, indicating that the mode of death had something to do with the pulmonary lesions. W. B.

Grossi, L., e **Da Rin, O.** Sulle modificazioni dell' indice opsonico provocate dalla tossina del bacillo di Pfeiffer nel decorso delle malattie acute e croniche. [**Changes of opsonic index caused by the toxin of Pfeiffer's bacillus during acute and chronic diseases.**] *Gazz. d. Osp.*, 1922, **43**, 403.

Experiments were made in rabbits with the following results: in animals infected with various germs (*Staphylococcus, Diplococcus, B. typhosus, B. tuberculosis*) the inoculation of the toxin of Pfeiffer's bacillus causes a remarkable diminution in the opsonic index and in the number of white blood corpuscles. The number of red blood corpuscles appears sometimes increased, sometimes diminished. These results remain unaltered whether the toxin is inoculated at the same time or after the infecting germs.

C. D. F.

Hudson, P. **Inoculation of white mice with Pfeiffer's bacillus.** *J. Infect. Dis.*, 1922, **30**, 433.

There has been a diversity of opinion on the action of *B. influenzae* on white mice. The present author found that it was pathogenic when injected intraperitoneally, the microbe being readily recovered from the heart blood. Strains isolated during influenza epidemics were particularly virulent, although the virulence was apparently not exalted by passage. Sublethal doses conferred an immunity against both heterologous and homologous strains, the immunity persisting for at least eight weeks.

W. B.

Howell, Katharine, M. **A study of two distinct strains of streptococcus isolated from the same heart-valve lesion.** *J. Infect. Dis.*, 1922, **30**, 299.

From the same aortic lesion in a case of chronic vegetative valvular endocarditis two strains of streptococci were isolated on blood-agar plates, one being a typical *S. haemolyticus*, the other *S. viridans*. On the basis of sugar reactions the haemolytic strain was *S. pyogenes*, the non-haemolytic strain being *S. salivarius*. The serological reactions also differed, all the characters originally present in the cultures remaining unchanged after two years' cultivation. When first isolated the haemolytic strain was much the more virulent, and agglutinated rather than laked blood corpuscles in fluid media. Both the virulence and agglutinating properties were lost during cultivation.

W. B.

Stevens, F. A., and **West, R.** **The peptase, lipase, and invertase of hemolytic streptococcus.** *J. Exper. M.*, 1922, **35**, 823.

The authors have studied the peptase, lipase, and invertase manufactured by the beta type of a haemolytic streptococcus originally obtained from a fatal case of peritonitis. The enzymes were obtained by grinding up the bodies of the centrifugalized cocci followed by extraction. The peptase was found to be active between P_H 4·4 and 8·7, with optimum action at P_H 7·2. In neutral phosphate solution its activity was destroyed at 57° C. in ten minutes. It was also inhibited by dilutions of gentian violet as high as 1 : 20,000. The invertase was active between P_H 5·0 and 8·0, with an optimum of P_H 7·0. Heating to 52° C. for ten minutes destroyed its activity. With the lipase the greatest activity was manifest at P_H 7·9, and it was completely destroyed at 55° C. in ten minutes.

W. B.

Olitsky, P. K., and Gates, F. L. Experimental studies of the nasopharyngeal secretions from influenza patients. VIII. Further observations on the cultural and morphological characters of *Bacterium pneumosintes*. *J. Exper. M.*, 1922, **35**, 813.

The work of the authors on the so-called *B. pneumosintes* has been previously referred to (*Medical Science*, 1921, **4**, 266, 560 ; **5**, 62, 1922, **6**, 238, 500). The present paper gives the results after three years' cultivation of the organism. The morphological and cultural characters have been maintained during this period, but the adaptation to a saprophytic life has been accompanied by loss of virulence. The strains, three in number, now grow readily under anaerobic conditions in a variety of media with peptone broth as a base, enriched with fresh tissue, blood, or by the growth of other bacteria. W. B.

Ditthorn, F. Über den Nachweis von Typhusbacillen in Butter. [**On the demonstration of typhoid bacilli in butter.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1922, **95**, 409.

In experiments hitherto performed it has been concluded that the viability of *B. typhosus* in butter is about 27 days. By means of bile enrichment methods the present author has shown that the typhoid bacillus was alive in butter up to 160 days and in margarine up to 126 days. W. B.

Peller, S., u. Russ, V. Beobachtungen bei einer Typhusepidemie unter Kindern. [**Observations of a typhoid epidemic among children.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1922, **95**, 135.

This is the record of an interesting epidemic of typhoid affecting chiefly children in a school in Austria and traced to a female carrier who was in charge of the kitchen. Sixty-one children were attacked and there were 25 other cases of contact infection, making a total of 86 cases. 87 per cent. of the whole series were children. Between 6 and 8 years every fourth child, between 9 and 10 every third child, and between 11 and 13 more than a third suffered from the disease. The paper also contains a record of the results of blood, stool, and urine examinations as well as the serological tests. W. B.

Howell, Katharine, M., and Schultz, O. T. An epizootic among guinea-pigs due to a paratyphoid B bacillus. *J. Infect. Dis.*, 1922, **30**, 516.

An account of an epizootic which led to the death of more than 500 guinea-pigs mostly with multiple tubercle-like lesions of liver and spleen. Females, and especially those that were pregnant, were peculiarly susceptible to the disease and purulent metritis was common. A bacillus of the typhoid-colon group was isolated which fermented xylose, arabinose, dulcitol readily, quickly formed alkali in milk, and darkened lead acetate agar within 24 hours. Immunologically the micro-organism was distinct from *B. paratyphosus* A and B, *B. enteritidis*, and *B. suipestifer*. It was highly pathogenic for guinea-pigs by ingestion or by subcutaneous, intraperitoneal, or intravenous inoculation. Although rabbits did not contract the disease spontaneously they were none the less susceptible to inoculation. W. B.

Smith, Theo., and **Smith, Dorothea, E.** **Inhibitory action of paratyphoid bacilli on the fermentation of lactose by *Bacillus coli*.** *J. Gen. Physiol.*, 1920, **3**, 21.

If a fermentation tube containing fermented bouillon plus 1 per cent. lactose is inoculated with some member of the paratyphoid group, the multiplication causes a heavy clouding or even turbidity in the open arm. If after four to six days' incubation the same tube is reinoculated with a true *B. coli* known to ferment lactose, one of two things may happen: (1) the resulting fermentation takes the usual course as if no prior inoculation had been made, i.e. the production of acid and gas goes on as in a fresh tube; (2) the second organism multiplies freely but no gas is produced, although titration shows that the usual amount of acid is produced. By means of this test the authors find that bacteria of the paratyphoid group fall into two classes. One class includes all true hog-cholera bacilli, the other nearly all true paratyphoid and *B. enteritidis* types. The activity of the inhibition factor was found to present itself in the form of a curve beginning at O when both paratyphoid and colon bacilli were inoculated simultaneously, and rising as *B. coli* is inoculated at longer intervals from *B. paratyphosus*. The maximum inhibition was reached at about the fourth day, thereafter it remains at the same level for a few days and then gradually falls until it is lost within three or four weeks. The authors tentatively present the hypothesis that the inhibitory factor is some metabolic product of the paratyphoid bacillus, possibly an enzyme which is destroyed at a temperature somewhat above the thermal death-point of the bacilli and gradually disappears from incubated cultures. The substance fails to traverse Berkefeld filters. It is carried down mechanically with substances, like kaolin, which clear the culture fluid. The experiments support the theory that the acid-producing and the gas-producing factors in cultures are distinct. W. B.

Trawinski, A. Ueber eine durch die Stäbchen aus der Gärtner-Gruppe hervorgerufene Meerschweinchenepidemie, mit besonderer Berücksichtigung der Morphologie und Biologie dieser Stäbchen. [**An epizootic, among guinea-pigs, caused by bacilli of the Gärtner group, with special reference to their morphology and biology.**] *Centralbl. f. Bakteriol.* (&c.), Abt. I, 1922, Orig. **88**, 24.

Description of a bacillus which was the cause of an epizootic among guinea-pigs in Paltauf's Institute in Vienna. The organism isolated was found to be closely allied to *B. enteritidis* by agglutinating tests, although the type of the colony and the pathogenic action was different from that produced by the latter micro-organism. W. B.

BIOCHEMISTRY

Kramer, B., Casparis, H., and **Howland, J.** **Ultraviolet radiation in rickets.** *Am. J. Dis. Child.*, 1922, **24**, 20.

Radiation by the mercury vapour quartz lamp increases the inorganic phosphorus content of the serum of rachitic children.

O. L. V. de W.

Kopeloff, N. Variations in aliquot fractions of gastric contents. *Arch. Int. Med.*, 1922, **30**, 118.

A wide variation was found in the acidity of 10 c.cm. fractions withdrawn in rapid succession by means of a Rehfuss tube. In fractions withdrawn simultaneously by three Rehfuss tubes at different depths in the stomach similar variations occurred, and a study of a natural regurgitator also led to the conclusion that the fractional method of gastric analysis is unreliable. O. L. V. de W.

Sisson, W. R., and **Denis, W. Chlorin content of cow's and goat's milk, and formulas commonly used in infant feeding.** *Am. J. Dis. Child.*, 1922, **23**, 431.

In 12 Jersey cows producing a relatively small amount of milk with a high fat content, the average chlorine content amounted to 175 mgm. per 100 c.cm., and showed remarkably small variations in the different animals. A dose of 500 grammes of salt produced practically no effect on the chlorine content of the milk. In 25 Holsteins, on the other hand, giving a very large yield of milk, the chlorine content varied from 75 to 156 mgm. Formulas used in infant feeding gave chlorine concentrations varying from 42 to 151 mgm. per 100 c.cm., as compared with a normal value for human milk of 40 to 60 mgm. The authors point out that formulas containing dextri-maltose with added salt may contain 400 per cent. more sodium chloride than human milk, and that pathologic gains of weight may result due to retention of water. O. L. V. de W.

Greenthal, K. M., and **Brown, G. M. Studies on the nature of non-specific protein in disease processes. IV. Blood fragility, reticulation, and blood chemistry.** *Arch. Int. Med.*, 1922, **30**, 99.

The non-specific protein dose varied from 100 to 750 million killed typhoid bacilli injected intravenously. A slight increase in the fragility of the red blood cells occurred during the paroxysm: there was no change in the percentage of reticulated erythrocytes. A moderate rise in the urea, and total non-protein nitrogen of the blood, were noted at the height of the fever. A slight rise in the blood-sugar and a fall of the alkali reserve of short duration were also noted. Certain differences between protein and anaphylactic shock are pointed out. O. L. V. de W.

Plaut, R. Gaswechseluntersuchungen bei Fettsucht und Hypophysiserkrankungen. [**Metabolism studies in obesity and diseases of the pituitary gland.**] *Deutsches Arch. f. klin. Med.*, 1922, **139**, 285.

The authoress has studied the basal metabolism in various conditions leading to obesity, and has compared it with the figures as given in the tables of Harris and Benedict (*A Biometric Study of Basal Metabolism in Man*, Carnegie Inst., Washington Publ. No. **279**, 1919), and has also investigated the specific dynamic action of food in these cases. The specific dynamic action can be decreased in cases of chronic under-nutrition and in obesity. In under-nutrition the decrease after food is a regulating mechanism which tends to conserve energy. When the specific dynamic action is low, independent of the condition of nutrition of the patient, laying on of fat takes place, and this is seen in diseases of the pituitary and especially in dystrophia adiposogenitalis.

Plaut thinks that the specific dynamic action of food is connected with the hypophysis, and as the result of her experiments believes that it is possible to distinguish by carefully conducted metabolism experiments between obesity of thyroid origin and one of constitutional or pituitary origin. She gives the following differential table :

	Basal Metabolism.	*Specific Dynamic Action.*
Under-nutrition	Normal or decreased	Decreased
Pituitary obesity or constitutional obesity	Normal	Decreased
Pituitary cachexia	Decreased	Decreased
Myxoedema and thyreogenic obesity	Decreased	Normal
Basedow's disease	Increased	Varies with condition of nutrition
Cachexia	Increased	?
Constitutional emaciation	Normal	Increased

C. G. L. W.

Grafe, E. Stoffwechseluntersuchungen bei Milz- und Lebererkrankungen. **[Metabolism in spleen and liver diseases.]** *Deutsches Arch. f. klin. Med.*, 1922, **139**, 354.

Total metabolism experiments on various conditions connected with pathological changes in the liver and spleen. They confirm the results obtained by American investigators that an increase in metabolism only takes place in primary cirrhosis of the liver, even when it is associated with large tumours of the spleen, when there is a considerable degree of anaemia present. In Banti's disease and splenomegaly of Gaucher's type the metabolism is increased without an associated anaemia. The indications for the extirpation of the spleen may be supported by basal metabolism estimations in the sense that a normal or slightly raised metabolism contra-indicates an operative interference. On the other hand, it needs a very considerable rise above the normal figures to indicate operative interference, because so many other factors come in which are of equal importance with the rise in metabolism. C. G. L. W.

Rosenthal, S. M. An improved method for using phenoltetrachlorphthalein as a liver-function test. *J. Pharmacol. & Exper. Therap.*, 1922, **19**, 385.

Experiments on dogs in which the liver function has been deranged by excessive doses of chloroform show that when the liver is damaged the amount of dye in the blood after intravenous injection reaches 15 to 30 or more per cent. and remains elevated for a prolonged period, while in the normal animal the amount in the blood falls to a trace within 15 minutes. There is evidence that the curves obtained have paralleled the degree of impairment of liver function, and it is believed that the method can be applied clinically. C. G. L. W.

Martin, C. J., and **Robison, R. The minimum nitrogen expenditure of man and the biological value of various proteins for human nutrition.** *Biochem. J.*, 1922, **16**, 407.

The question of the minimum nitrogen expenditure in man has always been a matter of great importance, owing to its connexion with questions of under-nutrition, and the authors point out that previous experiments have mostly been undertaken with some definite kind of protein. In the present experiments the authors have conducted tests upon themselves, using diets in which minimum quantities of cereal protein and the proteins of milk were used as sources of nitrogen. They find that the minimum nitrogen expenditure by the urine was 0·038 gm. and 0·035 gm. per kilo. The ratio of $\frac{\text{Body N Saved}}{\text{Body N Absorbed}}$ appears to remain constant, whatever amount of nitrogen is taken in the form of whole wheat bread, until equilibrium is reached. With milk the ratio may remain constant, but in the case of gelatine there is no indication that the amount of body nitrogen showed increase beyond that effected by the smallest quantity of gelatine fed. The mean biological value of the nitrogen in cow's milk in one experiment, in which an excess of calories was taken, was 51 per cent. The mean biological value for wheat grain was 35 per cent. for one observer and 31 per cent. for the other. C. G. L. W.

MANN, F. C., and MAGATH, T. B. Effect of the removal of the liver on the blood-sugar level. *Arch. Int. Med.*, 1922, **30**, 73.

The liver was removed in dogs by a technique devised by Mann. A marked and progressive decrease in the blood-sugar followed, and the glycogen content of the muscles decreased by 50 per cent. When a certain blood-sugar level was reached symptoms developed, and death occurred at a fairly constant point in relation to blood-sugar. O. L. V. de W.

LANDES, H. E., GARRISON, L. E., and MOORHEAD, J. J. A study in experimental diabetes. *Arch. Int. Med.*, 1922, **29**, 853.

The authors have investigated the effect of injections of pancreas perfusates on the course of the diabetes of depancreatized dogs. Glucose-free Tyrode solution was used for the perfusions. Attempts to estimate the effects of the perfusate by determinations of the D/N ratio failed, as the ratio was inconstant. The perfusates did not delay the onset of diabetes. Maximum glycosuria is delayed by injections of perfusates, but a compensatory rise in sugar excretion occurs later, and the delay is perhaps due to the action of depressor substances, shown to be present in the perfusates. Defibrinated blood from a depancreatized animal, passed once through a normal pancreas, had no effect on the experimental diabetes.

O. L. V. de W.

GRAFE, E., u. SALOMON, H. Über den Einfluss der Muskelarbeit auf die Intensität der Zuckerverbrennung beim Diabetiker. [**The influence of work on the intensity of the sugar utilization by the diabetic.**] *Deutsches Arch. f. klin. Med.*, 1922, **139**, 369.

The authors take up the important question of exercise in the treatment of diabetes and seek to supply information from the results of total metabolism experiments in diabetics before and after exercise. In only two cases was less sugar combusted after work than in the resting period. In all other cases there was a decided increase in the amount of sugar consumed. It would appear from these results that bodily activity, within reasonable limits, has a favourable influence in the therapy of diabetes.

The metabolism ran parallel with the amount of work done, but the work performed per unit of food was much less than that seen in normal subjects. These results show that the diabetic is not an economical person in the amount of work he performs for a given amount of potential energy.

C. G. L. W.

Zandrén, S. Ein Beitrag zur Frage der Bedeutung der pathologischen Aminoacidurie. [**The significance of the pathological excretion of amino-acids in the urine.**] *Ztschr. f. klin. Med.*, 1922, **94**, 1.

The excretion of amino-acids in the urine as a diagnostic sign of inefficient hepatic function has been studied by many observers without any definite conclusion being arrived at. The present author has utilized the formol method of titration to study the excretion of these acids in cirrhosis and tumours of the liver, in acute yellow atrophy, and in pregnancy. He finds that in cases of pronounced jaundice a normal excretion of amino-acids denotes a condition of damming back, while an increase is a sign of a serious hepatitis, and the method can be used for the early diagnosis of hepatitis or atrophy of the liver where the clinical symptoms only show a catarrhal jaundice. In pulmonary tuberculosis an estimation of amino-acids gives a better idea of the condition of the liver than does palpation or percussion. In cirrhosis of the liver an increase in amino-acids only takes place in the final stages of the disease when the clinical symptoms point to a contracted liver.

C. G. L. W.

Hedin, S. G. Die proteolytischen Enzyme des Eiweissharns. [**The proteolytic enzymes of urine containing albumin.**] *Ztschr. f. physiol. Chem.*, 1922, **119**, 264.

A protease is present in albumin-containing urine. If the urine is preserved in a slightly acid condition the action of the enzyme is stronger than when the urine has been kept faintly alkaline. The author explains this as being due to the presence of an inhibitory substance which is destroyed by acid. The alkaline urine has a strong inhibitory action on trypsin while the acid urine inhibits trypsin only very slightly.

H. W. D.

Schumm, O., u. Papendieck, A. Vorkommen und Nachweis von Tyrosin im Harn. [**Occurrence and detection of tyrosine in urine.**] *Ztschr. f. physiol. Chem.*, 1922, **121**, 1.

Tyrosine can be detected in urine by the methods of Frerichs-Städeler and von Lippich. The first will detect 0·2 gm. in 400 c.cm., and the second 0·01–0·02 gm. in 100 c.cm. Contrary to the commonly accepted view, the authors state that in numerous cases of undoubted acute atrophy of the liver no tyrosine, which can be detected chemically, is to be found in the urine. Crystals with the characteristic properties of tyrosine were found in the urine in one case of icterus catarrhalis and in one case of icterus following salvarsan administration (complicated by cystopyelitis), but only exceptionally in nine cases of acute atrophy of the liver. The mere microscopic examination of urinary sediments is useless for the identification of tyrosine.

H. W. D.

Williams, B. W., and **Dykes, S. C. Observations on creatinuria and glycosuria in myasthenia gravis.** *Q.J.M.*, 1922, **60**, 269.

In four cases of myasthenia gravis creatinuria was present, even on creatin-creatinin-free diet. Inability to deal with comparatively small amounts of creatin, given by mouth, was noted. In two cases a somewhat low muscle creatin percentage was found. Evidence of a low carbohydrate tolerance was obtained, as shown by an abnormally prolonged high blood-sugar curve after 100 gm. of glucose. Since laevulose produced no rise in the blood-sugar, it is suggested that the defect in carbohydrate metabolism is located in the muscles and not in the liver. O. L. V. de W.

Rabinovitch, I. M. Biochemical studies in a fatal case of methyl alcohol poisoning. *Arch. Int. Med.*, 1922, **29**, 820.

The patient died five days after drinking a glass of wood alcohol. The blood showed definite evidence of renal failure, a steady rise occurring in the uric acid, urea, and creatinin content. An increase in the reducing power of the blood was present, which might in part be attributed to the presence of formaldehyde, derived from the methyl alcohol, but which the author believes, in view of the work of Denis and Aldrich, was due to a true hyperglycaemia. The CO_2 combining power of the plasma fell to 26 vols. per cent. It is suggested that this may have been due to the formation of methylene derivatives, strongly acid in reaction, by the action of formaldehyde on the amino-acids present. Methyl alcohol was recovered from the tissues after death. The post-mortem examination showed parenchymatous nephritis, cloudy swelling of the heart and liver, and broncho-pneumonia.

O. L. V. de W.

Abderhalden, E., u. **Zorn, B.** Über die Zusammensetzung der Schuppen bei Psoriasis. [**The composition of the scales in psoriasis.**] *Ztschr. f. physiol. Chem.*, 1922, **120**, 214.

An analysis of the scales from a severe case of psoriasis was undertaken. Water and fat contents were determined and then a determination of the amino-acids was made. The results were as follow: alanine 4·5 per cent., serine 0·8 per cent., cystine 1·8 per cent., valine 3·2 per cent., leucine 5·2 per cent., glutaminic acid 6·5 per cent., phenylalanine 2·3 per cent., tyrosine 3·2 per cent., proline 3·0 per cent. The authors suggest that comparative estimations of the amino-acid content of the protein material in various skin diseases would be useful. H. W. D.

Schumm, O. Über das Porphyrin des Harns bei Bleivergiftung. [**Urinary porphyrin in lead poisoning.**] *Ztschr. f. physiol. Chem.*, 1922, **119**, 139.

The spectroscopic and physical properties of the porphyrin excreted in the urine in cases of lead poisoning show that it has the characteristics of faecal porphyrin and not of true urinary porphyrin, the latter not being present in detectable amounts. If this be the case it follows that the porphyrinuria of lead poisoning is not identical with that due to veronal.

H. W. D.

Sollmann, T. Studies of chronic intoxication on albino rats. VI. Lead carbonate. *J. Pharmacol. & Exper. Therap.*, 1922, **19**, 375.

The author gives a short summary of what is known with regard to lead poisoning in man and in animals. The amount necessary to produce intoxication in man is from 0·2 to 0·3 mgm. per kilo. The amount is much higher for animals. The experimental work was done on rats. Amounts from 0·0007 to 0·15 mgm. per kilo produced slight but definite check of growth and appetite. The mortality of these rats was high between 9 and 17 weeks, due probably to lowered resistance. The whole dose of lead in clinical human plumbism probably begins with one-fifth to one-third grain per kilo; but it is seen that much smaller doses are not harmless to rats, and it is pointed out that in cases of metallic poisoning there is probably a wide gap between the amounts which will produce definitely poisonous symptoms and those which are completely harmless. C. G. L. W.

Berger, W. Ueber die Hyperproteinämie nach Eiweissinjektionen. Ein experimenteller Beitrag zur Pathologie des Serumproteins und zur Proteinkörpertherapie. [B.] [**Excess of protein in the blood-serum after the injection of protein. The pathology of the serum proteins and of protein therapy.**] *Ztschr. f. d. ges. exper. Med.*, 1922, **28**, 1.

In an attempt to ascertain to what extent individual blood-proteins take part in the rise in these compounds which follows the injection of foreign albuminous compounds, the author has followed out analytically the amounts which occur in the serum after injection of foreign protein. He has also given some data with regard to the refraction, viscosity, and amounts of protein in the serum in untreated animals over a considerable period. The rise in protein in the blood-serum is due to the giving up of these compounds to the fluid from the body-cells. The first protein to increase is the fibrino-globulin, then the serum-globulin increases in quantity, and finally the albumin. From this he concludes that the three substances have different genetic origins. The rise in protein does not run parallel with the rise in precipitins after the injection of foreign proteins. He believes that the estimation of protein change in the blood as the result of protein therapy will eventually give information of importance both from a diagnostic and a prognostic point of view. A very full bibliography is given. C. G. L. W.

Freund, H., u. **Gottlieb, R.** Studien zur unspezifischen Reiztherapie. III. Mitteilung. [**Studies on therapy by non-specific stimuli. 3rd communication.**] *Arch. f. exper. Path. u. Pharmakol.*, 1922, **93**, 92.

Struck, H. Studien zur unspezifischen Reiztherapie. IV. Mitteilung. [**Studies on therapy by non-specific stimuli. 4th communication.**] *Arch. f. exper. Path. u. Pharmakol.*, 1922, **93**, 140.

These two papers represent a further attempt to investigate the scientific basis of that popular form of therapy in which serum or some protein preparation is injected into the circulation of the patient. In the first paper it is shown that an injection of serum produces a change in the response of the blood-pressure to adrenalin. When injections of adrenalin are made into a cat under ether on different days, the rise of pressure in mm. is approximately the same for any given dose, and the minimal effective dose is constant. After the injection of 20 c.cm. serum, the blood-pressure becomes in two or three days much more sensitive to adrenalin injections; the rise produced by a given dose is greater, and small doses previously ineffective become definitely pressor. Similarly (1) injections of serum, (2) injections of caseosan, (3) venesection, produce an increase in the amount of saliva excreted in response to a given dose of pilocarpine. This increase lasts as long as two months. The second paper shows that the substance in serum which has the power of restarting the beat of an isolated frog heart paralysed by muscarine, and which has therefore an action like atropine, is also one of the alcohol-soluble constituents of serum. It is not present in the circulating blood of healthy subjects, but is present in the blood from numerous hospital patients. J. H. B.

Fromherz, K. Über die Wirkung verschiedener Gruppen der Lokalanästhetika im Lichte verschiedener Untersuchungsmethoden. [**On the action of different groups of local anaesthetics as investigated by different methods.**] *Arch. f. exper. Path. u. Pharmakol.*, 1922, **93**, 34.

The author has investigated the action of novocaine, cocaine, and other patented preparations for producing local anaesthesia in four ways, (*a*) by testing their power to produce local anaesthesia (1) in the web of the frog's foot, (2) in the cornea of the rabbit; (*b*) by testing their power to stop conduction of the nervous impulse, (1) down the sciatic nerve of the rabbit, (2) down the sciatic nerve of the frog. He shows that a quantitative relation between two drugs expressing their power to produce anaesthesia in nerve-endings is entirely different from that expressing their power to suppress conduction. While novocaine is about as potent as cocaine for suppressing conduction in the nerve-trunk, it is much less powerful than cocaine on nerve-endings. The action of novocaine passes off quickly when the solution containing it is replaced by one not containing it. Novocaine is ineffective on mucous membranes because it so rapidly diffuses away.

J. H. B.

Langer, H. Die Desinfektionswirkung von Farbstoffmetall-Kombinationen. [**The antiseptic action of metal-dye compounds.**] *Ztschr. f. d. ges. exper. Med.*, 1922, **28**, 45.

The author believes that the combinations of metals with dyes which are used for disinfection in the body have their increased efficiency based on the increased dispersion which the metallic salt confers on the dye solution. At the same time the active metal is anchored to the dye molecule and in this way to the infected organism. C. G. L. W.

RADIOLOGY

Radiotechnique

Pissavy, A., et **Saidman, J.** Les injections radio-opaques en anatomie pathologique. [**The use of radio-opaque injections in anatomical pathology.**] *Presse méd.*, 1921, **29**, 494. (*J. de radiol. et d'électrol.*, 1921, **5**, 513.)

Very interesting pathological results can be obtained by the radiography of organs of which the vessels have been injected with substances opaque to X-rays. This method is particularly suitable in the following cases: vascular obliteration, the modifications in size of blood-vessels, and both the vascularization of tumours and the seat of haemorrhage in tumours. It can also be applied to the study of the resisting power of the blood-vessels, which, when ruptured by too great pressure, show dark and diffused patches, and also to the examination of such systems as the bile-ducts, the bronchial tubes, the ducts of the kidneys, and many of the glands.

Of the various prescriptions recommended, the following would appear to be, so far, the most suitable for the purpose: finely powdered red oxide of lead, salicylate of soda, essence of turpentine. *Directions.* Take the necessary quantity of salicylate (to be determined by the size of the organ to be injected), add oxide of lead in small quantities until a deposit settles at the bottom of the liquid, then add five drops of essence of turpentine. Give the injection by means of a container suspended at a suitable height to produce the necessary pressure. The injection lasts several hours, then the organ, hardened by formalin, is cut into slices an inch thick. If, in the same organ, one wishes to distinguish both veins and arteries, make two injections of varying density. Radiography is done in the ordinary way, and stereoscopic radiographs prove of exceptional interest. This method, applied to the study of the lungs, both normal and pathological, has yielded highly interesting results, which will be described at length in a forthcoming publication by one of these two authors. M. B. D.

Radiodiagnosis

Carelli et **Sordelli.** Un nouveau procédé pour explorer le rein. [**A new method for examining the kidneys.**] *Rev. Assoc. méd. argent.*, 1921, **34**, June. (*J. de radiol. et d'électrol.*, 1922, **6**, 97.)

A preliminary radiograph is made to locate the transverse apophysis of the second lumbar vertebra. A small-calibre needle, 10 cm. long, is then thrust in; when it touches the bone it is directed a little obliquely; at this moment, as the point is in the perirenal fat, the manometer connected with the needle oscillates slightly. The perirenal capsule is then injected with 200 to 400 c.cm. of CO_2 and a second radiograph taken. By this method the authors show the outline of the kidney, the ureters, and the suprarenals very clearly. The operation only causes a very slight malaise which disappears in less than half an hour. S. E. L.-B.

Szar, G. Le pneumothorax artificiel dans le diagnostic de l'abcès de foie. [**Artificial pneumothorax in the diagnosis of liver abscess.**] *Radiol. med.*, 1915, **2**, 422. (*J. de radiol. et d'électrol.*, 1922, **6**, 46.)

The author publishes three observations, two of which are illustrated. This method at once enables the existence of a cyst or intrathoracic or intrapleural tumour or collection of fluid to be excluded, and limits the differential diagnosis between a tumour and hepatic or subphrenic abscess. The presence of fever, the discoveries by palpation, the coexistence of dysentery, the persistence of the mobility of the right side of the diaphragm, which is wanting in the case of a subphrenic abscess, are of great use in settling the diagnosis. The introduction of the pneumothorax, however, is particularly useful when a serous or purulent pleural effusion is associated with the hepatic lesion; in such a case the introduction of gas will facilitate radioscopic reading of conditions of the diaphragm and hepatic cupola. The author does not believe that this method (Achard-Jacobeus) can always be recommended. The insufflation of gas is harmless when it is actually a question of a sub-diaphragmatic mass; but there is a risk of gas embolism when it is a question of an intrahepatic mass, especially if the pyogenic membrane be not sufficiently resistant. S. E. L.-B.

Papin et **Charrier.** Pyélographie dans la lithiase rénale. [**Pyelography in renal lithiasis.**] *Bull. Soc. franç. d'urol.*, 1920, Dec. 13. (*J. de radiol. et d'électrol.*, 1922, **6**, 48.)

The aim of this communication is chiefly to show the advantages of pyelography over simple radiography. In cases of calculus the injection of an opaque solution into the calyx indicates clearly the pelvic or intrarenal seat of the calculi and supplies indications for pyelotomy, nephrotomy, or even nephrectomy. In the discussion following the paper, Belot draws attention to the fact that, contrary to the author's opinion, the renal shadow can be made visible by means of a good technique in most cases (75 per cent.); with this visibility of the outline of the kidney, calculi can be localized with sufficient clinical accuracy without pyelography. S. E. L.-B.

Rossi, A. L'investigation radiologique dans le diagnostic différentiel entre la maladie de Barlow et le rachitisme. [**Radiological investigation in the differential diagnosis between Barlow's disease and rickets.**] *Radiol. med.*, 1921, **8**, 146. (*J. de radiol. et d'électrol.*, 1922, **6**, 140.)

(1) In advanced cases separation of the periosteum by a haematoma thickening of the extremity of the diaphysis of the tibia, bending of the posterior border, and bowing of the internal border are seen. (2) In the early stages in cases radiologically not rickets the 'partial sign of Fraenkel' is seen. (3) In early cases of rickets the differential diagnosis is difficult, but the presence of the 'partial sign of Fraenkel' and its rapid variability indicates the occurrence of Barlow's disease in a case of rickets. (4) In all cases the 'partial sign of Fraenkel' is associated with gingivitis and painful swelling of the knees. S. E. L.-B.

Ellis. Intestinal radiography in chronic appendicitis. *South African M. Rec.*, 1921, June 25. (*J. de radiol. ct d'électrol.*, 1922, **6**, 94.)

The passage of the opaque meal should be followed on the screen and recorded by a series of plates taken at intervals of 1, 3, 7, and 24 hours. A Lane's kink is almost always found, and the appendix may be clearly adherent to the terminal portion of the ileum. Often, however, the appendix is not visible, which fact should strongly suggest a chronic inflammation blocking or sclerosing the appendix. When the appendix is visible, a pathological condition is shown by kinks, by a clubbed shape, or irregularities of calibre. It often produces a marked slowing in the ileo-caecal region, with signs of dilatation in the lower portion of the ileum; sometimes the caecum or ascending colon is not visible; but a very constant sign is the kink and the sagging towards the right iliac fossa of the first part of the transverse colon, probably due to inflammatory adhesions arising from the appendix. There is usually a kink at the hepatic flexure and at some distance beyond (after the latter the transverse colon passes direct to the splenic flexure). These signs are often combined, but a diagnosis may be based on a few of them associated with a careful examination of the clinical symptoms. X-rays can be of great assistance when clinical examination alone does not permit of a diagnosis, if the above-mentioned syndrome be present.

S. E. L.-B.

Radiotherapy

Vallot, J. (Paris). Mesure de l'influence de la chaleur et de la lumière sur l'activité de réduction des tissus animaux, et application à l'héliothérapie. [**On the measure of influence exercised by light and heat on the reducing powers of animal tissues. Its application to heliotherapy.**] *Compt. rend. Acad. d. sc.*, 1921, **173**, 1196. (*J. de radiol. et d'électrol.*, 1922, **6**, 199.)

The object of this work is to study the influences of radiant heat, electric light, diffused light, and solar radiation upon animal tissues. The reducing power is very much decreased by bringing the temperature of the tissues lower than that of the average body temperature.

Feeble diffused light has but little action. Electric light, even when not powerful (½ Watt, 50 candle-power), at 15 centimetres' distance noticeably augments the activity. Solar radiation has a far more energetic action by reason of the cumulative effects of heat and light.

The author deduces from these experiments this practical conclusion: In order effectively to treat atonic ulcers by means of heliotherapy, the operator must not allow the activity of the tissues to be reduced by a diminution in temperature. The treatment must be given in an atmosphere which, although warm, is yet not hot enough to exceed the average temperature of the organism. M. B. D.

Lœper, Debray, et **Tonnet, J.** L'action de la radiothérapie sur le passage dans le sérum des albumines des tumeurs. [**The action of radiotherapy on the passage of the albumins of tumours into the blood.**] *Compt. rend. Soc. de biol.*, 1921, **85**, 279. (*Arch. d'électric. méd.*, 1921, **29**, 344.)

These authors, after working on the albumin passed into the blood by tumours, have been led to carry out researches as to whether X-rays augment the rate of passage of the albumin by their action on the tumour. They have estimated the albumin after carrying out intensive treatment on different tumours under identical conditions. On the whole they have found a constant increase in the albumin; the serum-albumin is unaltered, the globulin alone increasing in most cases. The increase in the albumin is rather rapid. The authors have found alongside with the increase in the volume of the albumin, a diminution in the amino-acids. They think that these facts tend to show that radiotherapy makes the albumin of the tumour pass into the blood and diminishes, especially for the first few days, the products of proteid metabolism and the erepsin. S. E. L.-B.

Barré, J. A., et **Gunsett, A.** Résultat de la radiothérapie dans 20 cas de radiculite causée par l'arthrite vertébrale (et en particulier dans la sciatique lombo-sacrée). [B.] [**The result of radiotherapy in 20 cases of radiculitis caused by vertebral arthritis (particularly in lumbo-sacral sciatica).**] *J. de radiol. et d'électrol.*, 1921, **5**, 492.

The authors state that radiological examination shows osseous or articular lesions very frequently in these cases. The twenty cases are divided into three series: (1) cases of complete cure manifested by the complete disappearance of painful symptoms: this includes twelve cases; (2) amelioration, less striking but distinct: this includes five cases; (3) cases which derived no benefit: this includes three cases. Short notes are given about each case. X-rays alone were used in treatment. The most favourable cases are those in which pain is the most marked sign: cases of meningeal origin do not appear to be influenced by radiotherapy. The duration of the disease does not seem to have much effect on the final result. In most cases a dose of 3 H. units filtered with 4 mm. of aluminium repeated every eight days is the best. In cases which do not respond to this treatment it is suggested that a dose of 10 H. units carefully applied might be used. P. L.-B.

Frankl, O., and **Amreich, I.** **Histological changes during the treatment of cancer of the uterus by X-rays and radium.** *J. Am. Coll. Surg.*, 1921, **33**, 162. (*J. de radiol. et d'électrol.*, 1922, **6**, 100.)

The authors assert a distinct difference between the action of the direct and indirect rays. The neoplastic cells react more rapidly to X-rays than to radium. The authors advise the use of X-rays in affections of the parametrium and of radium in ulcerating carcinoma. S. E. L.-B.

Radiobiology.

Bagg, H. J. **Disturbances in mammalian development produced by radium emanation.** *Am. J. Anat.*, 1922, **30**, 133.

The author begins by reviewing past work on the subject, from that of Bohn on the effects of radium upon the ova and larva of sea urchins, mentioning shortly the findings of each. His own experiments are mainly concerned with disturbances in mammalian development, before and after birth, resulting from the exposure of embryo rats to radium emanation at various times during the prenatal period. Female rats were also exposed before mating and the effects on the embryos studied.

Methods and apparatus. Two methods were used: in the first 'active deposit' was used, the method of employing it being described; pregnant rats were injected subcutaneously in the shoulder region and intravenously through the caudal vein: 3 to 4 minims was the usual dose, injected immediatedly after it was prepared. The solution exhibited all the phenomena of radium, but the author considers that the greatest physiological effect was probably due to the alpha rays: 5 millicuries was found to be the maximum dose applicable. In the second method gamma-ray irradiation was applied through the abdominal wall of pregnant rats at nearly full term. The method of application, the dosage, and filters used are fully described. About 1,300 millicuries produced developmental arrests in the embryos without killing the mother: doses up to 2,900 millicurie hours were used in some cases. The embryos were killed by ether: histological material was procured at various times after treatment, fixed in Bouin's solution, cut in serial section, and stained with haematoxylin and eosin.

Experimental results. *Series A. Injections of radio-active solutions. I. Subcutaneous after mating.* Sixty-five rats treated in four groups: ten 7 days after mating, twenty-four 10–14 days after mating, twenty-one 15–17 days after mating, and ten 18–21 days after mating. Many animals were killed at weekly intervals, but some reached full term. The developmental disturbances were grouped as follows: (1) In many cases no embryos developed, in others many began development, but absorption or abortion occurred later. Those in which no embryos were found were irradiated soon after mating. (2) Embryos were killed by the treatment, but were removed before they were absorbed. These showed various extravasations from the vessels of the subcutaneous connective tissue, within the meningeal sinuses and mainly along the dorsal midline. Not all the foetuses in a litter were affected to the same degree; this was considered to be due either to the higher or lower vitality of the embryos or to the amount of radio-activity which passed the placenta. (3) Several young of a single litter showed areas of extravasation and were born alive, but the mother died. (4) Eight litters gave normal living young; this number is low because many animals were killed as stated above. The average number per litter was 4·8 as compared with 6·5 per litter in the controls, but probably this is not significant. Only one litter of four young survived a treatment given seven days after mating. Several rats in this group, which had apparently escaped the full exposure during the uterine period, when mated together produced litters of apparently normal fertile young, whose offspring for two generations were observed without abnormalities being found. *II. Subcutaneous before mating.* Seventy-seven females used; eleven died after injection before mating; several killed at weekly intervals after mating; some continued to full term. Thirty-four animals injected 5 and 7 days before, seventeen 10–14 days before, and fifteen 20 days before mating. Only three litters showed abnormal young. The lesions were extravasations as before but more widely distributed and more variable in size than in section I. Usually the female was rendered sterile or the young were killed and absorbed early. The lesions found in the three litters referred to above are described. Seventeen females were killed at varying intervals after mating, and showed markedly haemorrhagic or cystic ovaries and congestion of the uterus: nodules were found in the uteri in which it was impossible to differentiate between maternal and embryonic structures. The offspring of those animals that went to full term were kept under observation under the same conditions as in section I and produced no abnormal offspring. *III. Intravenous after mating.* The object of these was to determine the immediate reactions that might occur in the embryo after injecting a large dose of radio-active solution into a pregnant female, and whether the results, if any, were similar to those produced by subcutaneous injection. The toxic reaction was very prompt and fatal: a typical case is recorded in which three young were born dead twenty-four hours after the injection with definite radium changes as described above.

Series B. Results from radiating nearly full-term pregnant rats with gamma-ray radiation. Ten rats were treated after about 19 days of pregnancy: 1,350 mc. hrs. of radium emanation produced very decided changes in the embryo and left the pregnant females able to suckle their young. A dose of 3,378 mc. hrs. severely injured the young, which were either killed outright or died 2–3 days after birth. The following are the conditions that resulted in the first generation of animals treated *in utero* with a dose of about 1,350 mc. hrs.: (1) in each case the young were born 2–3 days after radiation, apparently normal; (2) about 10 days after treatment about half of each litter became anaemic and died, showing slowly developed meningeal and cord haemorrhages as described as a result of the injections of radio-active solutions. Histologically the most marked pathological lesions were fatty degeneration of the liver-cells and desquamation of the lining cells of the intestinal mucosa; (3) the other half of each litter grew to normal size and some lived for 18 months, showing certain arrests in development: (*a*) the eyes were smaller, the pupils opaque, the lids became closed, and finally complete blindness resulted; (*b*) in the first lots both sexes were sterile; later, however, a first generation female mated with a male, each having been treated with 1,350 mc. hrs., gave birth to 9 apparently normal young; (*c*) except for blindness there was nothing to suggest abnormal sensory function; (*d*) post-mortem examination showed great developmental disturbances in the central nervous system; these are described; (*e*) the eyeball was one-fourth the normal diameter; retina was missing, but traces of the choroid remained; the cornea was three times as thick as normal and covered with opaque squamous epithelium; the optic nerve was small; (*f*) the testes were very atrophic, epididymis practically missing: little evidence of spermatogenesis was seen. The ovaries were reduced to one-fourth or one-fifth the normal size; Graafian follicles were entirely absent.

Control group. Rats in the same condition, of the same weight and age as the above, were injected subcutaneously and intravenously with equal amounts of solutions which, previously strongly radio-active, had been allowed to 'decay': the results were completely negative. As a control to the radiation experiments, sister rats were allowed to breed under the same experimental conditions: no abnormal young were observed,

Discussion and summary of results. The author considers that the extravasations found were probably due to the destructive action of radium on the endothelium of the vessels and also possibly to an increase in blood-pressure. Other authors are referred to in connexion with this. The experiments show that a sufficient quantity of radio-activity could pass through the placenta and subsequently affect the embryo: the author does not attempt to explain how the lesions occurred in the embryos when the mother was treated a considerable time before mating; he only concludes that for some reason it lessens the faculty of the embryo to form proper endothelium. The intravenous injections show that the placenta may act as a 'shock absorber'. The results of the gamma-ray experiments show the delayed reaction associated with this type of radiation. The effect on the intestinal mucosa is in line with the results of Whipple and Hall in their experiments on X-ray intoxication in dogs (*Medical Science*, 1922 **6**, 262). That some young of a litter died and some lived may be due to individual susceptibility to or tolerance for the radiation, but is probably due, according to the author, to the fact that some embryos would be farther from the source of radiation than others. Even the animals that survived the ten-day period suffered from the effects of the radiation; the chief effect was on the neopallium, which never recovered its proper rate of development in relation to the other parts of the brain. The author believes it was an actual inhibitory effect on the nerve-cells. The physiological functions of the cerebral cortex of the rat were apparently transferred to the basal ganglia, &c., showing a remarkable degree of compensation in the mammalian brain when disturbed early in development. Ovaries and testes appeared to suffer equally. Organs which had differentiated before the radiation was employed apparently developed normally; the author considers that earlier antenatal treatments should throw light upon the critical growth periods of the various embryonic structures. He also points out that there is good experimental evidence to show that spermatozoa of some animals, after comparatively small exposures to irradiation, are likely to produce abnormal young. He draws the attention of clinicians and laboratory workers to this last observation, and the attention of physicians to the possibility of producing developmental arrests when treating pregnant women, and also to the possibility of altering the germ-cells by irradiation previous to conception.

The paper is accompanied by ten figures and three plates illustrating the lesions described in the text. P. L.-B.

MEDICAL SCIENCE

ABSTRACTS & REVIEWS

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NOTICE.

In the references the letter [B] after the title signifies that the original memoir contains a good bibliography of the subject dealt with.

REVIEWS

PNEUMONIA

Symptomatology. Coleman has observed in some very serious, and as a rule fatal, cases of lobar pneumonia a *peculiar type of respiratory movement* characterized by a dissociation of the contraction of the diaphragm and of the intercostal muscles. 'The diaphragm contracts first, the abdomen protrudes, and then, after varying intervals, contractions of the intercostal muscles follow. The lowermost intercostals may contract first, and the movement of the thorax progresses like a wave from below upward, or the delay in the contraction of the intercostals may result in complete asynchronism. In the fully developed type of asynchronism the diaphragm reaches the expiratory phase before the contractions of the intercostals set in, and the abdomen and chest rise and fall alternately—" see-saw " best describes the impression conveyed'. Dilatation of the alae nasi occurs before the bulging of the abdomen. Various degrees of this dissociation of movements of the abdomen and the intercostals are noted in different cases, and Coleman gives tracings showing 'asynchronism'.

No final explanation of the phenomenon presents itself, but Coleman suggests that it may be due to unequal depression of the bulbar (formatio reticularis) or other centres by the toxin of the pneumococcus. The sign indicates a grave prognosis.

Lyon has studied the clinical aspects of 208 cases of *pneumonia in infants and children* up to the age of 12, which were seen at the Boston City Hospital between February 1919 and February 1921. Eleven cases of pneumonia in influenza are not considered. Lobar pneumonia was quite common even in the youngest patients, and altogether there were 109 cases of lobar and 99 cases of lobular pneumonia. In the lobar cases the mortality increased with the age of the child. There were 12 cases in infants under 2 years of age, but no deaths; 28 cases in children between the third and fifth years with no deaths; and 69 cases in those from 6 to 12 years old with a death-rate of 7·3 per cent. The cases of lobular pneumonia give quite a different picture of mortality. The greatest number of cases and the highest death-rate occurred in infants under 2 years of age, for there were 52 cases, and 50 per cent. of these died. The death-rate shows a gradual fall instead of a rise with increasing age as seen amongst the lobar cases. There were 25 cases in children 3 to 5 years old, with a death-rate of 28 per cent., and 22 cases in those from 6 to 12 years of age, of whom 9·1 per cent. died. The death-rate in all cases of broncho-pneumonia amounted to 35·4 per cent., and it will be seen that it is a much more serious disease to be reckoned with in children than lobar pneumonia. The death-rate in all the cases of pneumonia was 19·2 per cent.

Lobes affected in cases of lobar pneumonia. As Lyon says, other writers have described a much higher incidence of consolidation of the upper lobes (especially the right) in lobar pneumonia in children than is shown by his own figures of: right upper 24, right lower 38, left upper 2, left lower 29, and more than one lobe affected 14 cases.

Certain points about the *clinical features of the lobar cases* described by Lyon are of interest. Diminution of the breath-sounds is often the only sign over the affected lobe, and Lyon found it very useful to corroborate his clinical findings by examining the chest with the fluoroscope. Generally speaking, there was little tendency for the disease to spread to another lobe. Cough was not so troublesome as in the cases of broncho-pneumonia. Pain was very often referred to the abdomen and vomiting was common. Cyanosis occurred in only 9 per cent. of the cases. The disease in four cases lasted more than eleven days without complication. The temperature fell in the majority of cases on the sixth or seventh day. Crisis occurred in 40 per cent. of the cases. The white blood count was noted in 91 of the 109 cases, but except to help in diagnosing empyema it was of little value in determining prognosis.

Empyema headed the list of complications of the lobar cases. It occurred in six patients (5·5 per cent. of the cases), all of whom recovered after operation. As a matter of routine, the ears of children suffering from pneumonia should be examined. *Otitis media* occurred in five (4·6 per cent.) of the children. In one child lobar pneumonia recurred in the left lower lobe, but the pneumonia was due to a different type of pneumococcus.

Broncho-pneumonia. In the cases of broncho-pneumonia consolidation was much more common in the lower lobes. In 73 of the 99 cases it was double. In many cases marked changes in the physical signs were noted after the lapse of a few hours, and extension or migration of the consolidation were often described. X-rays were of great value in detecting signs of consolidation. As a rule, the symptoms developed gradually; vomiting was common, but sharp pleuritic pain was not noted as often as in the cases of lobar pneumonia. Cyanosis was three times as common as in the lobar cases, and was seen in 27·2 per cent. of the cases.

The *duration* of the disease was more difficult to reckon than in the cases of lobar pneumonia, for broncho-pneumonia is so much more insidious in its onset. Twenty-four cases lasted 7 days or less, 6 lasted from 7 to 14 days, and 3 cases lasted more than 28 days. The temperature curve was much more irregular than in the lobar cases. Decline by lysis was the rule, but in 2 cases crisis occurred. Again the white blood count helped little in prognosis, but was useful in detecting complications.

In 62 cases with adequate histories the broncho-pneumonia was secondary to some other disease such as 'colds', pertussis, measles, tonsillitis, acute laryngitis, acute otitis media, mumps, erysipelas, syphilis, furunculosis, typhoid fever, or, as in one case, it followed tonsillectomy.

Empyema occurred in five cases (5 per cent.), and four of these died, *acute otitis media* thirteen times (13·7 per cent.), and acute fibrinous *pericarditis* once. *Diphtheria* followed three cases of broncho-pneumonia.

Lyon concludes that the prognosis in pneumonia of children is worse the younger the child, and that it is grave if there is much diarrhoea or if the child has rickets. The death-rate is high, especially in pneumonias following measles, pertussis, and diphtheria.

Nobel discusses the difficulty of diagnosing *pneumonia in weaklings and premature babies.* As Rommel has pointed out, these infants may die of asphyxia during the first few days after birth, and a haemorrhagic form of pneumonia be found at autopsy, although the disease had run an afebrile course. Finkelstein is of opinion that a genuine fibrinous pneumonia does not occur before the fourth or fifth month, and in the case of the lobular variety he quite rightly lays more stress upon the general symptoms of septic intoxication than upon the localizing signs. From his own clinical experience Nobel confirms Ducken's opinion that X-ray examination in cases of pneumonia amongst the new-born is often of little value, for in cases where clinical examination left no doubt that pneumonia was present and the diagnosis was confirmed at autopsy, the X-ray had shown no change or very much less than was really the case.

Often pneumonia cannot be diagnosed by the direct method of localizing symptoms and signs, but by the indirect method which a consideration of the general signs of an infection makes possible. A peculiar grey coloration of the skin or a mixture of pallor and cyanosis may be the most important sign, or there may be cyanosis accompanied by attacks of asphyxia. Fever is generally notable by its absence, and a low temperature accompanied by a marked disturbance in heat regulation is common. This latter is often revealed in a striking way when an infant with subnormal temperature is placed in the warming chamber, for the baby may immediately become very feverish, dyspnoeic, and cyanotic. Frequency of respiration is seldom, in Nobel's opinion, a reliable sign, but the type of breathing with gasping or groaning expiration and inspiratory retraction of the intercostal spaces may lead one to the diagnosis. Dilating alae nasi is an inconsistent sign. Another of the most important general signs is loss of appetite accompanied by sudden loss of weight. Snuffling and sneezing are often noted. At times the infant vomits bile-stained or blood-stained fluid, or there may be frequent watery and slimy stools. Signs of disturbance of the heart and circulation are very uncertain.

Signs of *meningism,* such as restless movements of the hands, stiffness of the neck, loss of consciousness, bulging of the fontanelles, and deep breathing (probably all caused by oedema of the brain) may make one suspect meningitis or cerebral haemorrhage. Examination of the lungs often leaves the physician uncertain, as merely a diffuse bronchitis may be recognized. On the other hand, there may be dullness over the upper lobes accompanied by bronchial breathing, and a case diagnosed pneumonia during life turn out after death to be extensive atelectasis. As Professor Schick has pointed out, when a diagnosis of 'debilitas vitae' is made in cases of weaklings and premature infants a pneumonia is very frequently found at the post-mortem examination. *Prophylaxis.* Nobel claims that by keeping the babies and their mothers in small rooms and not exposed to the catarrhal infections of the upper respiratory tract so frequent in a large crowded ward, the infant death-rate could be much lowered.

Up to the present it has not been sufficiently recognized how often and quite unexpectedly pneumonia is found as the cause of *deaths occurring immediately after birth.* In Brown's series of 80 deaths in infants, 21, or 26·25 per cent., were due to pneumonia. Eleven deaths were of premature and 9 of full-time infants who were from 8 hours up to 9 weeks old. If it is taken that there is one premature to every 10 full-time infants, then the premature is 14 times more liable to die of pneumonia. Five of the babies were syphilitic and another probably was, so syphilis may be reckoned as a possible determining factor. Atelectasis was found *post mortem* in many of the cases, especially among the premature. It is probable that premature rupture of the foetal membranes may allow infection of the child during expulsion, for Brown cites two such cases of fatal pneumonia, and the condition of grey hepatization found at autopsy showed that infection must have occurred before the child was born. In the first instance, death occurred eight hours after birth, and catarrhal pneumonia was found and an organism of the pneumo-bacillus group grown from the lung. The second case was of three days' duration with post-mortem findings of empyema, hepatization of the right lung (greyish-red marbling), small abscesses of the left lower lobe, and tricuspid endocarditis. Cultures from the lung, heart, and pus in the pleural cavities gave a pure growth of *B. coli.* (It is not stated whether cultures were taken from the vegetations.)

Several kinds of lesions were found in the pneumonic lung, such as *catarrhal pneumonia*, which accounted for half of all the deaths, but the most interesting form is *acute haemorrhagic pneumonia* described at length by Browne. At six of the twenty-one post-mortems a condition of congestion with more or less oedema of the lung associated with haemorrhages into the alveoli and bronchi were found. In five of these instances the lung was otherwise healthy, but in the sixth there was also a precedent interstitial pneumonia. The haemorrhage in the lungs always appeared fresh, and had evidently occurred just before death, which had been sudden in four cases. In three of these death was preceded by epistaxis. There was little associated catarrhal pneumonia, but sometimes intense oedema accompanied the congestion. Browne is as yet unable to explain fully the cause of the congestion during which (as the microscopic picture shows) the fragile foetal vessels in the walls of the alveoli break away and allow haemorrhage into the air-cells. Neither syphilis nor prematurity is a necessary factor, as of the six fatal cases only one was in a syphilitic baby and only four were premature. Cultures were made from three cases: in one there was a *B. coli* infection, in another *Staphylococcus aureus* was grown, but in the third the cultures were negative, and no organisms could be seen in sections of the lung stained by Gram's method. In this case death occurred with a dramatic suddenness. Half an hour before the child was found dead in bed with frothy blood exuding from its nose and staining the pillow, it was regarded as in perfect health by the nurse. The thymus, as seen *post mortem,* was enlarged, and Browne suggests that anaphylaxis may have been the cause of the acute congestion, oedema, and intrapulmonary haemorrhage.

Thompson deals briefly with *recurrence of lobar pneumonia* in the same person. One robust man of 35 had attacks every year for three years with intervals of 18 and 13 months respectively. No influenza was epidemic during these years. On each occasion the onset and physical signs were typical of lobar pneumonia. In the first attack the crisis occurred on the 6th day, and in the second attack on the 5th day, but expectations were not fulfilled in the third attack, as termination was by lysis from the 8th to the 10th day. The left lower lobe was consolidated in the first two attacks and the right upper in the last one. In another patient—a male aged 24—who had two attacks of lobar pneumonia, with an interval of eleven months, termination was by crisis in both instances. In the first instance crisis occurred on the 5th day, with precipitous fall of the temperature curve from 105° to 97° in twelve hours, followed by a rebound to 100° for two days. On the second occasion the crisis was slower and occurred on the 8th day, again followed by a rebound, but this time to 99° only. Unfortunately, details of the type of pneumococcus found on the several occasions in these two patients are not given by Thompson, and until such statistics are available discussion of temperature and immunological reactions are not possible. There should be no better opportunity of clearing up our ideas about the mode of recovery (e. g. the bactericidal and detoxifying factors: see *Medical Science*, 1921, **3**, 513–15) in pneumonia than a close study of all the data provided by successive attacks of lobar pneumonia in the same patient.

In a recent Paris thesis André has described the natural history of *dissecting pneumonia*, drawing upon seven cases in the French literature and adding to the number a fresh one of his own. The French mind requires that all facts be systematically and logically arranged, but we might perhaps be content to speak of this 'dissecting pneumonia' as a sequela or complication of some cases of atypical pneumonia, as we regard gangrene of the lung, which condition it closely resembles. There is nothing of importance in the previous history of the patients beyond the fact that some of them had had attacks of bronchitis. There is often a chill and sharp pleuritic pain at the outset, dyspnoea, cough, and irregular fever. Two forms of the disease are distinguished: 'dissecting peribronchitis', already described by Hutinel and Proust, in which after a few days signs of consolidation of part of one or more lobes appear. The expectoration is haemorrhagic and purulent, and sometimes large amounts are brought up after a fit of coughing, and after a couple of weeks elastic tissue and other signs of destruction and cavity appear. In the other form, 'diffuse subpleural phlegmon', the end result—cavitation—is the same, but the disease seems to begin as a 'subpleural lymphangitis' and the pulmonary signs are often masked by a purulent pleural effusion, and pyopneumothorax may result; or after operation for empyema portions of necrosed lung may come away and the diagnosis is made. The prognosis in the former class of case is very grave, but less so in the latter. In the majority of cases death occurs in six to eight weeks. Post-mortem appearances of the lungs are described. In some cases a whole lobe is converted into a cavity, with ragged walls, crossed by blood-vessels and containing portions of neurotic tissue. Microscopic examination may show that organization of patches of pneumonia has occurred in some places, whilst in others necrosis only is found. Bronchietasis is found in other parts. Perilobular fibrosis—an attempt at healing—is common in the second form. There may be areas of haemorrhage. X-ray examination may suggest an intrapleural empyema, but later a cavity containing fluid can be made out and sometimes destruction of a whole lobe is clearly seen.

Friedländer's bacillus is the most common cause, but a large number of other organisms have been isolated, the most important of which seems to be the streptococcus.

With Hutinel and Proust, André considers that 'dissecting pneumonia' differs only in degree from gangrene of the lung. In the former foetid sputum does not occur so early.

In the light of the recent work of MacCallum (vide *Medical Science*, 1920, **2**, 16–17) and others on interstitial pneumonia, we can see that cases of 'dissecting pneumonia' are similar to it, and that the infection in such cases passes out from the hilum of the lung along the lymphatics of the supporting tissues, and under certain conditions—not yet fully understood—abscesses are formed as well as patches of hepatization; small haemorrhages are seen also, and finally, probably following thrombosis, gangrene supervenes. In the second class of case infection extends rapidly along the lymphatics to the pleural cavity and a purulent pleurisy or empyema occurs almost at once.

Complications. Foster reminds us that *pericarditis* in lobar pneumonia may sometimes be due to streptococcus and not to a pneumococcus. If it is recognized, by a to-and-fro friction rub, that pericarditis has begun, and if it is known later that fluid has developed, it is difficult to say with certainty whether this is ' simple fluid ' or infected fluid or pus. The pericardial sac must be explored with the needle. In principle, treatment of empyema of the pericardium is the same as empyema of the pleura. We must not wait until the patient is exhausted by infection before we begin to deal with these complications.

Empyema occurred in 6 per cent. of Foster's civil hospital cases and more frequently in the army patient suffering from pneumonia. The two important varieties of empyema are those caused by the pneumococcus and by the streptococcus. In the former the empyema does not generally involve the whole pleural cavity, but from the onset is walled off. In streptococcal cases adhesions are of later formation and numerous small walled-off cavities may result. A primary interlobar pocket arising from a streptococcal interstitial pneumonia may rupture into the general pleural cavity.

The first difficulty met with in the treatment of empyema is that the condition is often not recognized. Foster believes that this is due to two facts: (1) it is not necessary to have a ' typical ' chart with a fall of temperature followed by a rise, and (2) the physical signs are so misleading. Foster finds it necessary to plead for the use of the needle in diagnosing an empyema.

In *streptococcal empyemas* the lowest death-rate occurs if early aspiration and late operation are done. Repeated aspirations with every rise of temperature are generally required. If after ten to fourteen days the patients do not continue to improve, or if the pus becomes too thick for aspiration, a rib must be resected. A few cases require no such operation. On the other hand, in *pneumococcal empyemas,* where the pus is thicker, the best results are sometimes obtained if thoracotomy is done at once. Some patients seem to stand the shock of operation better if aspiration is performed first. There is seldom a cure by aspiration alone.

Pulmonary abscess is not a frequent complication of pneumonia and its diagnosis is always fraught with difficulty. Foster thinks the X-ray, especially a stereoscopic picture, is more useful in diagnosing this condition than it is in detecting an empyema. There are usually no adhesions if the abscess is centrally placed, and the treatment of choice is to collapse the lung by producing an artificial pneumothorax. Foster had the opportunity of seeing the autopsy performed on a man who had died of chronic nephritis, and in whom a pulmonary abscess had been treated by this method six years before. The area of the abscess was entirely replaced by fibrous tissue. If the abscess is closer to the surface of the lung, adhesions to the parietal pleura are generally present and collapse by means of artificial pneumothorax is impossible. In such cases, incision of the abscess or lobectomy should be attempted by a skilled surgeon. Foster states that the death-rate in such cases should not exceed 10 per cent.

Phlebitis is a rare complication of pneumonia, and in 1912 Gaultier and Pierre found only sixteen cases in the literature. Mya, in 1891, was able to isolate the pneumococcus from the thrombus in such a case. Martelli reports the case of a man, aged 23, who had a very severe attack of pneumonia of the left lung. His pulse became very irregular, and there were signs of failure of the heart, but a typical crisis occurred on the ninth day. Two weeks later, when resolution was almost complete, the patient complained of severe pain in the left groin which radiated down the inner side of the thigh and leg. His temperature rose to 100·4°. On examination, it was found that the left internal saphenous vein was thrombosed. After ten days the pain had entirely disappeared, the intermittent temperature had become normal, and no further trouble was experienced. The saphenous, or femoral, veins are the most frequently affected. In other reported cases the axillary vein was involved. Martelli suggests two factors in the causation of this condition: (1) poor circulation owing to myocardial weakness, and (2) circulating toxins, or perhaps pneumococci, which injure the endothelial lining of the vein.

Acute arteritis, followed by thrombosis and gangrene of the part supplied, has quite often been described in small-pox, rheumatic fever, influenza, gonorrhoea, and cerebrospinal meningitis. Head reviews the literature, and shows how relatively infrequent this complication is in pneumonia. In Douillet's patient, aged 21, the posterior tibial artery became thrombosed two days after defervescence. Gangrene set in and the leg was amputated. Recovery followed. Fussel describes a case of thrombosis of the interosseous arteries of the hand occurring after the crisis of lobar pneumonia in a man 41 years old. The process extended upwards. Gangrene followed and the patient died. Brouardel and Géroux reported a case of a woman of 58 who had thrombosis in the right brachial artery arising on the seventh day of lobar pneumonia. The radial pulse was lost, there was tenderness along the brachial artery, the arm was ischaemic, but the collateral circulation sufficed to prevent gangrene.

Head gives an account of two fresh cases. Three days after the crisis of lobar pneumonia a young negro soldier had a severe pain in his right leg and knee, the pulsation in the dorsalis pedis ceased, and subsequently gangrene set in and the leg had to be amputated above the knee. There was extensive thrombosis in the right femoral and popliteal arteries, and microscopic examination revealed definite evidence of arteritis. Head's second case was one of localized gangrene of the skin of the toes coming on in a young man of 26 whilst convalescing from an attack of bronchopneumonia. Recovery followed without operation. In neither of these cases were any lesions of the heart made out.

Arthritis. Cramer and Piotrowski discuss the articular manifestations of pneumonia. Arthritis is the most infrequent complication of the disease. It may precede, accompany, or follow any pneumococcal infection elsewhere in the body, but this latter is generally a pneumonia. Also pneumococcal arthritis may, on very rare occasions, exist as the only evidence of a pneumococcal infection. As in typhoid the majority of the cases of arthritis in pneumonia occur during convalescence. The arthritis may appear in a joint, the resistance of which has been lowered by a previous injury or disease, such as gout.

Cramer and Piotrowski have reviewed 35 cases in the literature. Fourteen showed involvement of the shoulder-joint, 14 of the knee, 2 of the wrist, 2 of the ankle, 1 of the elbow, 1 of the metatarsal-phalangeal, and 1 of the metacarpal-phalangeal joints. These authors have determined the frequency of the complications in 7,421 cases of pneumonia. Their own cases are included in these figures. The complication occurred in the proportion of 1·9 to every 1,000 cases of pneumonia.

They distinguish six forms of arthritic complications. (1) *Arthralgia*, with fleeting pains, which soon disappear and no trace of trouble remains. (2) *Serous*, in which there is an effusion of clear fluid containing pneumococci. (3) *Plastic*, which is comparable with gonorrhoeal plastic arthritis, but the prognosis is not so grave for return of function in the pneumococcal form. (4) *Suppurative*, which is the most common; the joint contains greenish-coloured pus, but the symptoms are not as acute as in other kinds of suppurative arthritis. (5) *Osteo-arthritis*, where there may be destruction of ligaments, of synovial membrane, and of the periosteum. There is great redness, swelling, sharp pain, and marked rise of temperature. (6) *Periarthritis*, i. e. bursitis and tenosynovitis.

The authors' own cases comprise 3 of arthralgia and 5 of suppurative arthritis, which occurred at the Hôpital Cantonal de Genève between 1897 and 1917. The arthritis was mono-articular in 4 cases and poly-articular in 4. The shoulder was affected four times, the knee-joint three times, the great toe once, the ankle-joint once, and the temporo-maxillary once. The onset of the symptoms of the milder arthralgic form was on the fourth to fourteenth day, but in the suppurative form it was considerably later in the course of pneumonia—i. e. on the twelfth to seventeenth day. The physical condition of the patients was not good; two had had syphilis and 6 were confirmed alcoholics. The death-rate amongst these cases, amounting to 50 per cent., was not wholly due to the arthritis, but also to the severity of the pneumonia or to another complication such as empyema, meningitis, or pericarditis.

Johnston and Morgan report a very remarkable case of *acute lobar pneumonia and haematogenous puerperal infection*. A primipara, aged 35, who gave a history of having had numerous infectious diseases, was admitted during the first stage of labour after having walked some distance in a drenching rain. The temperature was normal, and examination of the heart and lungs revealed no abnormality. The second stage of labour was prolonged and a deeply-asphyxiated child was delivered by means of a 'low forceps operation' under chloroform anaesthesia. Almost immediately afterwards the patient's temperature began to rise, and in a few hours' time reached 104°; she complained of slight pain in the right side of the chest and a soft pleural friction was audible. But there had been no chill, cough, or bloody sputum, and the breathing was not quickened until 24 hours after delivery. Abdominal examination was negative. The next day there were signs of commencing consolidation of the left lower lobe, and the abdomen was distended and sensitive. On the second day the blood-culture was reported positive for Type I pneumococcus (173 colonies per c.cm. of blood). On this day, by means of a Little's tube, lochia, for intra-uterine culture, were obtained, and a Type I organism isolated from this also. Subsequently, the discharge from the uterus was of a greenish colour, and contained numerous pneumococci of the same type. On the third day fresh consolidation of the right lower lobe was made out and the white blood cells numbered 6,250 per c.mm., thus showing a poor resistance to the infection.

Intravenous treatment with Type I antipneumococcal serum was begun; 200 c.cm. being given on the third and fourth days of disease and 100 c.cm. on the sixth, seventh, and eighth. There was no systemic reaction to the serum, but eight hours after giving the first dose the number of pneumococci in the blood had fallen to 3 per c.cm., and blood-cultures were negative after the second dose and remained so. The leucocytes had risen to 18,000 per c.mm. The patient's general condition was much better after the serum treatment, but the temperature remained elevated. A greenish muco-purulent vaginal discharge persisted, and there was still some tenderness in the pelvis on abdominal and rectal examination. One week after the onset of the pneumonia the lochia contained a moderate number of leucocytes and lancet-shaped diplococci and Type I pneumococci were obtained in pure culture.

The condition of the patient remained the same for about two weeks more, with the temperature, pulse, and number of leucocytes still elevated. There was less tenderness in the pelvis, and two weeks after parturition a slight vaginal discharge persisted, but was sterile.

The condition now seemed to be one of 'delayed resolution' and the endometritis appeared to be a thing of the past. Examination of the chest suggested encapsulated fluid high up in the right axilla, and the X-rays showed 'remains of consolidation at the right base with suggestion of encapsulated fluid in the right axilla'. In the course of the next few days the patient again became gravely ill with high fever, weak pulse, and drenching sweats. The thorax was explored several times but no fluid was obtained. Blood-culture gave 7,600 colonies of streptococci per c.cm.; pelvic examination was negative. Death occurred nineteen days after delivery. Unfortunately, no post-mortem was permitted. The authors consider that there can be no doubt that the endometritis was haematogenous and that the post-partum uterus constituted a *locus minoris resistentiae* towards a pneumococcal bacteriaemia. The literature on haematogenous and vaginal puerperal infection with the pneumococcus is discussed, but most of the data on the subject are necessarily rather unreliable, for only of late years has the separation of pneumococci from streptococci been possible.

Treatment. Herrick considers that *oxygen unsaturation* or anoxaemia, which brings about grave disturbances in cellular metabolism, is a more important factor to contend with in lobar pneumonia than failure of the right heart. The former is partly responsible for the latter. Instead of administering it as a last resort, oxygen should be given in large quantities by 'insufflation or one of its effective modifications' at frequent intervals from the beginning of the disease to every patient who shows any cyanosis or other evidence of anoxaemia.

Herrick employs small doses of *digitalis* as a routine, but is not convinced that the drug is useful except in patients with chronic myocardial weakness or auricular fibrillation.

He finds that camphor and ether, whisky, and camphor in oil are of little use. With Lieb (*Arch. Int. Med.*, 1917, **19**, 811), he has shown that these and kindred substances apparently obtain their effects by irritation of the endings of sensory nerves rather than by any direct effect on the circulation. If the afferent sensory tracts were severed and then the drugs mentioned above injected into the limb, no change in the pulse or blood-pressure occurred. Herrick believes that in some cases of lobar pneumonia with marked abdominal distension due to toxic paresis of the bowel, *pituitrin*, deeply injected into the vessels at the same time as a turpentine enema is given, may save life.

Serum treatment. Thomas has written a valuable paper on pneumonia caused by Type I pnemococcus and the results of treatment with specific serum. Excluding figures of cases in the Rockefeller Institute series reported by Cole (*J. Am. M. Ass.*, 1921, **76**, 111–12) and others, Thomas gives the statistics of cases occurring in St. Luke's Hospital, New York, and of those described in the literature since 1916 (chiefly reports of base hospitals in the War). Pneumonia associated with influenza is not considered.

During 4½ years since January 1, 1917, there were 306 cases of lobar pneumonia in the adult wards of St. Luke's Hospital. Certain facts are noteworthy. The incidence of the four types of pneumococcal infection varies from season to season. There were a relatively large number of Type I cases in the first half of 1921—25 out of a total of 47 cases—whilst for the whole period of 4½ years the Type I cases amounted to 25·1 per cent. only. During the period of 18 months (1918–19) Type II cases were conspicuous by their absence, and this period included that covered by the influenza epidemic. The continued predominance of Type IV cases over those caused by other types is so remarkable that Thomas suggests that this form of pneumonia is endemic, whilst a Type I infection is epidemic in character. No system of comparing statistics has been thoroughly carried out, but Thomas reaches the important conclusion that 'the mortality rate of acute lobar pneumonia appears to vary with the time and place of its occurrence'. If this is so, and the death-rate in Type I cases may vary from time to time, then it is readily seen how difficult it is to appraise the result of any specific form of treatment.

Altogether, Thomas deals with 610 cases of Type I lobar pneumonia from the literature and from St. Luke's Hospital; 177 of these were treated without serum. Doubtless they were mild cases, but they must needs be considered for what they are worth if we are to make any comparison in the results of different forms of treatment. The specific treatment was omitted in those cases at St. Luke's Hospital when the patients were admitted very late in the course of the disease. The death-rate amongst those who received no serum was 12·9 per cent., and amongst those who were treated with serum it was 11·3 per cent. Thomas's enthusiasm for serum treatment has moderated a little, but he still feels that certain patients were greatly benefited by its use. In 4 cases out of 50 treated at St. Luke's Hospital it appeared to cut short the disease. In one of these there was a favourable crisis after two injections of 100 c.cm. A temporary benefit resulted in 8, and the duration of the disease was apparently not affected in the remaining 38 cases.

Sometimes there was an immediate drop of temperature after the injection of serum, but a relapse followed and the case finished just as is usual in those patients who received no serum. A chill with rise of temperature after the injection was noted in 14 cases, and a rise of temperature without chill in 6 cases. The remaining 30 cases exhibited no thermal reaction, nor was there any demonstrable effect on the course of the disease. Seven cases showed delayed resolution. Several patients had a relapse, and a different type of pneumococcus (II, III, or IV) was isolated from the sputum. As an additional skin test before giving the serum, Thomas suggests the use of the protein of horse dandruff, for it has been shown that an asthmatic may be sensitive to this substance and not to horse-serum given intradermally. In such a case a severe reaction may follow an intravenous dose of horse-serum. It must be remembered that two cases of anaphylactic death following injections of antipneumococcal serum have been reported in the literature. In some instances it is impossible to desensitize the patient. 36 of the 50 patients suffered from serum sickness

(i. e. a delayed reaction), which was quite severe in 12 and accompanied by urticarial eruptions, joint-pains, and, in some cases, nausea and vomiting. Epinephrin gives temporary relief in such cases. The average duration of the serum sickness was 6 days.

Amongst the 10 cases not treated with serum, termination was by crisis in 2 and by lysis in 8; among the 40 cases treated with serum the corresponding figures were 13 and 27. By 'crisis', Thomas means a fall, within 24 hours, of the temperature, which then remains down.

Herrick considers the position in regard to treatment of Type I lobar pneumonia with Type I antiserum. This was employed very widely in American military hospitals in 1918 and 1919. None of the physicians with whom Herrick spoke were opposed to it and one was very enthusiastic in its favour. The majority considered that the treatment should be given a trial until much more data is accumulated. Herrick's own opinion is that the serum should be given as early as possible in all cases of Type I lobar pneumonia. It seems possible that later on a better and more concentrated serum, free from objectionable serum proteins and containing antibodies for all the pathogenic types of pneumococci, will be found, so that the present typing methods will not be necessary. Herrick considers that, given before the third day, Type I antiserum may cut short the attack so that the defervescence occurs on the second to fourth day. Given later, the effects are generally not so striking but are often very favourable.

All cases of Type I lobar pneumonia, in the opinion of Niles, should receive Type I antiserum except (1) young children, in whom intoxication is not great and who are difficult to treat by intravenous injection; (2) adults with slight toxaemia seen for the first time late in the disease who are improving; and (3) elderly patients. The mortality in patients with Type I lobar pneumonia who do not receive serum treatment is about 25 per cent. (but compare Thomas's lower figures above). In several series of treated cases it has been below 10 per cent. Niles thinks that reports of ill success, when analysed, showed that the treatment was not carried out properly, for (1) insufficient doses may have been given : merely 25 to 30 c.cm. when 80 to 100 c.cm. are required ; (2) infrequent doses, only once every 24 or 48 hours instead of every 8 hours; and (3) inaccurate typing, so that conclusions drawn as to results of treatment must necessarily be false and useless for purposes of comparison.

McGuire also outlines some of the principal reasons why favourable results are not always obtained after the use of Type I antipneumococcal serum in Type I lobar pneumonia. (1) The serum is not given early enough in the course of the disease, for it has been repeatedly shown that the earlier treatment is begun the lower is the death-rate. (2) An attempt is made to treat the serious cases only; this is unreasonable, for a mild case may at any time take a turn for the worse. (3) With Niles, he considers that often insufficient serum is administered. No definite limit can be set, and it must be given until the desired effect has been obtained. Even as much as 1,000 c.cm. may be necessary (Cole), but in the majority of cases 200 to 300 c.cm. will suffice. It is best given every 8 to 12 hours in doses of 100 c.cm. Of course, if the skin test shows that the patient is sensitive to horse-serum, he must be desensitized (see *Medical Science*, 1920, **2**, 23). (4) The type of pneumococcus is not determined in every case; this operation requires about 12 hours; if no sputum is obtainable, McGuire punctures the lung to get material for the culture. (5) Some physicians use so-called 'polyvalent serum' and not specific Type I serum. McGuire states that so far no serum but that for Type I has proved its worth (contrast view of Sacquépée below); therefore he condemns the use of polyvalent serum.

The most striking results of the treatment with Type I serum in McGuire's 35 cases was that on the average the febrile period of the disease lasted for 66 hours only.

According to Sacquépée, Truche, in France, has prepared antiserum which has proved useful in the treatment of Type I and Type II cases, but not for Type III cases. Nicolle and Debains (*Bull. Acad. de Méd.*, May 24, 1919), and also Sacquépée, have found that Type II pneumococcus is by far the most common cause of lobar pneumonia in France and after it Type III. Type I is found very infrequently. On account of these figures Sacquépée commences the treatment of his cases by injecting a mixture of 2 parts of Type II and 1 part of Type I antiserum. Later, when the organism has been isolated from the sputum and the type determined, the specific serum alone is employed.

The best mode of giving antiserum is directly in a vein, although the subcutaneous, intramuscular, intratracheal, and even intrapulmonary methods have been tried. In the United States 90 to 100 c.cm. are given every 8 hours, but Sacquépée commences with 40 c.cm., and injects 60 c.cm. on subsequent days if necessary. Intradermal tests of minute doses are required at first to learn whether the patient is hypersensitive. If so, he must be carefully desensitized with gradually increasing amounts, at first given subcutaneously and later intravenously, every half-hour. The serum should be diluted in 8 to 10 volumes of normal saline, given at body-temperature, and administered very slowly.

Sacquépée noted no very serious reactions amongst his cases; two had severe chills occurring a short time after the injection, and several others had slight chills. A *serum reaction* appeared in some of the patients about the 7th to 12th day after the first injection. This was characterized by urticaria, local oedema of the upper lip and root of the nose, a morbilliform rash, and some pain about the joints. The patients were young, active soldiers, in whom the mortality is generally about 9·20 per cent. if no serum is used. Sacquépée had two deaths in 37 cases (5·4 per cent.), and in one of these the disease was caused by a Type III pneumococcus. The duration of the disease was definitely shortened, the temperature sometimes fell immediately after the first or second dose and stayed down, or it might rise again for a short time, and in a third class of case defervescence was very gradual. Even if the temperature is not greatly affected the patient seems more comfortable and the signs of toxaemia less striking.

Intratracheal injections were employed by Rathery and Mathieu during the War in the treatment of the pulmonary lesions following the inhalation of poison gases, and later others tried the method in cases of influenzal pneumonia. Without claiming too much for the form of treatment, Robert describes his methods of administering gomenol oil. A laryngeal catheter is used or the oil is injected with a syringe by thrusting the point of the needle through the cricothyroid membrane to a depth of 10 to 25 mm. thus ensuring that the lumen of the trachea has been reached but not crossed. Ten minutes before the actual injection of the oil 0·5 c.cm. of 1:10 or 1:20 solution of cocaine is injected by way of anaesthetic. 10 c.cm. of a 2 to 5 per cent. solution (Robert sometimes employed a 10 per cent. one) of gomenol oil are injected. No cough is caused. The patient is instructed to breathe through the nose and not to talk. Seven cases of broncho-pneumonia were treated in this way in the autumn of 1919 and winter of 1920, and only one died. The earlier the injection, the better the result. Robert noted a great lessening of dyspnoea and cyanosis, and generally there was a rapid fall of temperature.

Robert also describes an experiment performed on an animal, which showed that the oil reached the lung of the side on which the animal lay. Large amounts of the oil had entered the alveoli and very little remained in the bronchi.

Combined treatment with horse-serum and venesection. Bingel states that there is no doubt that in some cases of pneumonia, especially influenzal pneumonia, injections of horse-serum have a very favourable influence upon the course of the disease; in other cases good results are not obtained. It is the same story with venesection; sometimes it is of benefit, sometimes not. Bingel is convinced that a combination of these two methods of treatment is very valuable. He describes a series of 20 cases of lobar pneumonia so treated in which death seemed imminent. Horse-serum (12 to 20 c.cm.) was given intramuscularly, and a couple of hours later about 600 c.cm. of blood were withdrawn from a vein, and a few hours later horse-serum was again given. Generally crisis or lysis set in the following day. In a few instances there was a recurrence of fever, but the combined treatment was instituted again and good results were brought about. Bingel admits that in these cases camphor and other drugs were also used 'as seemed necessary', but is of the opinion that recovery was not wholly due to them. He throws out the suggestion that without a subsequent venesection the foreign proteins of the horse-serum remain in the tissues, but later, owing to the withdrawal of blood, they more easily reach the active circulation and exert their influence upon the pulmonary lesions.

Arterial section. Eckstein and Noeggerath state that up till now, as far as they know, no one except Baginsky has employed arterial section instead of venesection to unload the heart rapidly in cases of failure of the lesser and general circulation in pneumonia, and especially in oedema of the lung. In 1898, Baginsky compared the rapidly beneficial effects upon the circulation obtained by arterial section to the immediate benefits to the breathing when a tracheotomy is done in cases where a foreign body is lodged in the glottis. Favourable results of the method have been reported by surgeons in the War in rapidly relieving oedema of the lungs following the inhalation of poison gases.

The author states that the method is peculiarly advantageous in young children where (1) the veins are very small, and if collapsed, as often is the case in pneumonia, only a few c.cm. of blood can be obtained even by cutting veins in several places; (2) in a fat child it is difficult to find the vein on cutting down. They do not favour Moore's method of cutting the cephalic vein owing to the danger of air embolism. When transfusion of arterial blood has been done it has been shown that the radial artery can be tied without causing permanent damage to the circulation, as anastomosis in the hand is so rich. The advantages of unloading the heart quickly by arterial section easily outweigh the very small chance of gangrene of the hand occurring.

The radial artery is exposed a finger's breadth above the wrist-joint by a longitudinal incision; the artery is cut into, allowing the required amount of blood to flow; and the vessel is tied above and below to forestall secondary haemorrhage, although in some cases mere compression above permanently arrests bleeding. No anaesthetic is required, and in a fraction of a minute —much more quickly than by venesection—the required amount of blood is obtained.

So far they have employed this method in five cases. One of these was in a child, 4½ years old who had been poisoned with digipuratum—oedema of the lungs resulting. Immediate relief followed. The subjects of the other three cases were children 1 to 2 years old, with rickety chests. They showed failure of the lesser circulation in broncho-pneumonia accompanied by pulmonary oedema; 70 to 150 c.cm. of blood were withdrawn and very favourable results obtained. The fifth case was in a child of 18 months, who had had influenza and had entered the hospital with bronchitis of some weeks' standing. The child was vomiting, there were signs of a general infection, and red blood cells were present in the urine. Oedema of the lungs set in with collapse of the circulation. After 70 c.cm. of blood were taken off, the condition of the circulation improved, but the child died in two hours. At the autopsy no pneumonia was found, but oedema of the brain, evidently an end result of a generalized infection.

For adults the authors suggest taking away 5 c.cm. of blood per kilogramme of body-weight. Where rapid withdrawal of the blood is necessary, and impossible by venesection on account of a very feeble circulation, the method is indicated.

Protein therapy has become very popular for all kinds of diseases, and it is right, as Neumann says, that we should take stock of our ideas and study the results very critically. Theoretically, the mode of action of foreign protein given parenterally is that it stimulates the body-cells to greater function, especially in the manufacture of protective substances. It is not known definitely whether the foreign protein itself, decomposition products of the cells of the body, or ferments are the active agent.

Neumann employed 'Caseosan', introduced by Lindig, to replace ordinary milk. It is a 5 per cent. sterilized solution of casein, is put up in ampoules ready for use, and, comparatively speaking, causes a mild reaction. It is well known that the effects are produced more rapidly if the foreign protein is given intravenously, so this method was adopted by Neumann in treating such acute diseases as lobar pneumonia, except for patients who were extremely toxic, and then intramuscular injections were employed.

The initial dose was 0·25 c.cm., 0·5 c.cm., or 1 c.cm. On the other hand, as much as 2·3 c.cm. can be given intramuscularly. 'Caseosan' was never given more than once a day, and the number of doses for the individual patients of this series varied from 1 to 5. A marked reaction which occurred in some cases consisted of a severe chill, accompanied by unpleasant subjective sensations followed in about half an hour by a rapid rise in temperature. After an hour, or a few hours at the most, there was generally a drenching sweat and a critical fall of temperature, which was either of temporary duration only (followed by a rapid rise), or, as is generally the case, this fall led to a distinct change in the type of temperature curve, so that, instead of being continuous, the fever became markedly remittent. It was repeatedly noted that the critical fall of temperature was accompanied by phenomena of collapse as may be seen after a true crisis. In one instance these lasted for some time and gave rise to anxiety. Often, however, the injections (especially intramuscular ones) brought about no reaction. In cases where the doses were spaced out at intervals of several days no anaphylactic phenomena were seen. Headache, nausea, or vomiting were sometimes occasioned, whilst the patients in other instances experienced a sense of well-being or a pleasant feeling of tiredness.

Neumann treated 22 cases of lobar pneumonia, which he divides into 12 'early cases', where treatment was begun on the fourth day of disease or earlier; and 10 'late cases', in which the foreign protein was not given until after the fourth day. Full charts of the results are given, and the reader is referred to the original article for these. Neumann quite rightly recognizes that it is extremely difficult to set the proper value upon any form of treatment in lobar pneumonia, seeing how suddenly and without interference of any kind the whole outlook for a particular case may suddenly change.

In only one of the 12 'early cases' could Neumann attribute the favourable outcome to the injection of the protein. In 5 cases the result of treatment was uncertain, and in 6 cases the 'Caseosan' apparently had no influence at all on the course of the disease. In the 10 'late cases' a relatively favourable influence was noted twice. Of course, Neumann realizes that the defervescence, even in these two cases, may have been spontaneous, for in the majority of untreated cases this phenomenon generally occurs somewhere between the 5th and 10th day. In 4 cases the effect of the treatment was uncertain, and in the same number no influence one way or the other could be detected. There were two deaths in this series of 22 cases—a relatively low death-rate of 9·5 per cent.—but it must be borne in mind that the series is small. Neumann concludes that treatment with foreign protein offers no great advantage in pneumonia and has decided to discontinue it. On the other hand, we can see that his conclusion might not necessarily apply to other forms of foreign protein treatment, such as the injection of peptone or bacillary protein. Neumann admits that 'Caseosan' exerted a favourable influence on some of his cases of erysipelas.

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A. M.

TYPHUS

Epidemiology. Hoare, lately assistant lecturer in the Academy of Medicine at Petrograd, gives a *résumé* of the reports presented to the All-Russian Congress on typhus fever in Petrograd in 1920, which embodied the results of investigations made in Russia during the epidemic of 1918–20, during which period Russia was completely isolated from other countries. According to Fedorov, during the epidemic of 1918–19 47,333 persons contracted the disease, of whom 4,352 died—a mortality of 9·2 per cent. The mild character of the disease in children is shown by the fact that of 353 children admitted to hospital with typhus only two died, a mortality of 0·6 per cent. (Khalutina). Children of 12 years of age were most commonly attacked. In older children the disease tended to assume the type seen in the adult.

Migai states that during the World War the total number of cases of typhus in the Russian Army was 27,064. In the Red Army the condition was satisfactory until October 1918. From that date until April 1919 47,181 cases were registered in the Red Army, in which the disease developed after an outbreak in the civilian population. The mortality from typhus in the army ranged from 2·9 to 3·9 per cent., as compared with 9 per cent. in the civilian population. As usual, the mortality was highest among the medical officers, as 67 died out of 515 who contracted the disease (see also *Medical Science*, 1920, **1**, 561).

According to Prokofieff, the total number of cases of typhus notified at

Moscow during the years 1918–20 amounted to 104,119, which were distributed as follows: 1918, 7,217 cases; 1919, 74,752 cases; 1920, 22,150 cases. Owing to the disorganization of the sanitary service at this time these figures should probably be doubled. During the three years four epidemic waves were noted, the first being from January to August 1918, the second from September 1918 to August 1919, the third from September 1919 to August 1920, and the fourth from September 1920 until May 1921. The epidemic of 1918–19 was particularly severe, there being about 900–1,000 fresh cases notified daily in March 1919.

Sternberg, of Petrograd, draws attention to the remarkable fact that in spite of the prevalence of starvation as well as of the lack of the most essential hygienic requirements, such as drainage, closets, and baths, the course of infectious diseases in Petrograd during the period 1917–19 was not more severe than in previous years. Thus the mortality from typhus in the Petrograd hospitals was 9·4 per cent. in 1918, and 11·8 per cent. in 1919 as compared with an average mortality of 12·2 per cent. during the last 30 years. Sternberg attributes this occurrence to premature senescence produced by starvation through changes in the endocrine glands, with the result that the character of the infectious diseases was so modified that the illness ran a less violent course than in younger persons.

Hutter describes an epidemic of typhus which occurred in the prisoner's camp at Krasnozarsh in January 1920 after the defeat of the Siberian White Army by the Bolshevists. A combination of circumstances favoured the outbreak, viz. the entrance of the Red Army into a town already overflowing with refugees and sick, introduction of the Communist régime with depreciation of the Siberian currency, closure of the market, and confiscation of wood, with subsequent starvation and lack of fuel. The epidemic reached its height in March and began to subside in May. The mortality was about 17 per cent. Almost all the sanitary staff were attacked, mainly as the result of an artificial infection with defibrinated blood from typhus patients, which was carried out by an enthusiastic Hungarian medical officer for the purpose of prophylactic vaccination (see *Medical Science*, 1919–20, **1**, 567–8). The failure of the method was attributed to the fact that the required temperature of 60° C. was either not obtained at all in the thermostat available or was not maintained for a sufficiently long time. Hutter, who was vaccinated twice, had a comparatively mild attack, but most of the cases had a very severe illness and several died, while only a few of those inoculated remained healthy.

Shattuck examined the records of the Boston City Hospital from 1911 to 1921 and found that during that time four cases were diagnosed as typhus. It is probable that a few cases escaped detection, the records indicating that the possibility of typhus was not considered.

According to Borzone, head of the Sanitary Commission sent by the Argentine Department of Hygiene to the Calchaqué valleys in the province of Salta, typhus is endemic in this region and in the cold season is liable to assume epidemic form with a mortality ranging from 15 to 20 per cent. Nothing is known as to the epoch at which the disease first appeared, but it has probably existed in the north-west Argentine from time immemorial.

Aetiology. In the report of the Typhus Research Commission of the League of Red Cross Societies to Poland, Wolbach, Todd, and Palfrey, as the result of careful researches carried out under exceptionally favourable conditions, come to the conclusion that *Rickettsia prowakezi* is the cause of typhus. Their most important evidence is that contained in the experiments showing that the virus of typhus and *Rickettsia prowazeki* are inseparable in infective lice. Next in importance is the presence of bodies indistinguishable from *Rickettsia prowazeki* in the lesions of man. Commenting on the work of these American observers, Nattan-Larrier concludes that in spite of their failure to culture *Rickettsia prowazeki* none of the organisms hitherto described as the causal agent of typhus has so many demonstrative facts or rigorous experiments in its favour as *Rickettsia prowazeki.*

Symptomatology. Schrötter draws attention to a hitherto undescribed phenomenon in typhus, viz. *hyperexcitabitity of the muscles* by mechanical stimuli, which is shown by short, sharp, and sometimes even gentle taps on the most sensitive muscles, such as the biceps, triceps, supinator longus, or tibialis anticus, producing a hard projecting lump at the area stimulated of the character of idiomuscular contraction. The lump comes up rapidly and subsides slowly, lasting from 4 to 6 seconds. The sign appears on the fourth or sixth day and is most pronounced at the height of the disease. Schrötter attributes it to increased permeability of the capillaries, which favours the action of specific poisons on the muscle substance. Histological examination of the affected muscle shows Zenker's waxy degeneration.

Daniélopolu, of Bucharest, disputes Devaux's claim to have been the first to describe the *changes in the cerebrospinal fluid* in typhus, and states that in March 1917, or nearly a month before Devaux, he had drawn attention to the intense meningeal reaction which corresponds to the nervous symptoms present in the disease. He had pointed out that the fluid in such cases might be clear or turbid, in severe cases it had a yellow colour, and in hypertoxic forms it coagulated. In almost 50 per cent. of the cases Noguchi's reaction was present, and in 75 per cent. there was a cellular reaction which was usually intense. On naked-eye examination the brain presented an oedematous appearance with haemorrhages scattered over the meninges.

Benhamou, Jahier, and Barthélemy, of Algiers, who treated more than 200 cases of typhus during the winter of 1920–2 found that *nitrogen retention* was not only more frequent in typhus than in any other infectious disease, being present in more than half the cases, but reached a higher figure than any previously noted (8·80 gm. in one case). Clinically, nitrogen retention was the accompaniment of the so-called 'nervous form' of typhus, for which the designation 'azotaemic form' should be substituted. A systematic examination of the urea in the blood of typhus patients showed that nitrogen retention was accompanied by the following symptoms indicating its presence: motor restlessness, tremors usually confined to the upper limbs, especially the hands, and, in more pronounced cases, epileptiform attacks of the Jacksonian type. Other early signs of nitrogen retention were mental dullness, extreme prostration, and loss of flesh. The most important guide, however, for the detection of azotaemia is the condition of the urine. The writers recommend that when there is relative or absolute oliguria the dosage of urea in the blood should be measured, anuria being the final stage of nitrogen retention. The prognostic value of nitrogen retention was shown by the fact that patients with an amount of blood urea below 0·50 gm. recovered with rare exceptions, whereas the prognosis was unfavourable with more than 0·88 gm. of urea in the blood or cerebrospinal fluid of old persons, or above 1·70 gm. in the prime of life. When the amount exceeded 2 gm. the outlook was usually hopeless.

In a paper based on 224 cases observed in the epidemic of 1919–20, Herzenberg, of Moscow, states that the *surgical complications* of typhus occur in a more or less definite succession, and may be divided into an early and a later group. The number of complications is almost nil up to the eighth day of disease, when they begin to rise in frequency until the fifteenth day, when there is a slight fall until the eighteenth. There is then a fairly steep rise until the twenty-fifth day, then a daily decline until the thirty-fifth, when there is another small rise, the number of complications falling to zero on the fortieth day. Children are more or less immune to complications, whereas persons of advanced age succumb before the stage of complications is reached.

In a review of recent Russian work on typhus, Cheinisse states that Roubachev, of Kharkow, estimated that one out of three typhus patients developed some form of surgical complication, whereas in typhoid fever the proportion was 1 in 10, and in relapsing fever was still less. Complications of the soft parts, such as boils, cutaneous or subcutaneous abscesses, and cellulitis, were the most frequent, and then, in order of frequency, vascular lesions, lesions of bone, parotitis, and lesions of the lymphatic system. Other complications were much less frequent. Gangrene of the lower limbs in typhus has been much commoner in Russia during the last few years than in all previous epidemics. Dmetrev is quoted as having observed this complication in 173 out of 9,239 cases of typhus. Only 13 of the 173 recovered. Spondylitis, which is well known as a complication of typhoid fever under the name of ‘ typhoid spine ’ was noted as a complication of typhus by Roubachev and Totzky. According to Roubachev, spondylitis following typhus is much milder than typhoid spine, whereas Totzky considers that the clinical symptoms and pathological characters of the complication are the same in both diseases. Dodine is quoted as having recorded 15 cases of a hitherto undescribed complication of typhus, which consists in paralysis of the branches of the recurrent laryngeal nerve supplying the crico-arytenoideus posticus, as shown by inspiratory dyspnoea, which may be sufficiently severe to require tracheotomy.

Dobrovolskaia, professor of surgery at Voronege, in Russia, states that during the epidemic of 1919–20 a large number of *costal complications* occurred among the refugees from South Russia and proved extremely refractory to ordinary treatment. The onset of the costal lesion took place in convalescence or two or three months after the attack of typhus. Tuberculosis appeared to be the predisposing cause in most cases, while syphilis was a less frequent factor. Dobrovolskaia maintains that this form of osteochondritis was not due to secondary infection, as no growth was obtained from the pus on ordinary media. Conservative treatment combined with intramuscular injection of iodoform was employed with success.

Fraenkel, of the Pathological Institute of Hamburg University, records a case of typhus in a youth aged 17, in whom the cause of death was *perforative peritonitis* due to a necrotic change in the fundus of the stomach. Microscopical examination of the affected part showed considerable disease of the arterial wall characteristic of typhus, involving not only the intima but also the muscular coat. A definite typhus nodule had not been formed, although here and there an increase of the adventitia cells had taken place.

Recent clinical descriptions of typhus will also be found in the chapter by Shattuck in the monograph by Strong and his collaborators, as well as in the work by Wolbach, Todd, and Palfrey, in which the more important symptoms and complications of 181 severe cases are tabulated.

Diagnosis. Delamare (1) employed Friedberger's skin reaction (see *Medical Science,* 1920, **1**, 563–4; 1921, **4**, 197) in 5 cases of typhus, 14 of typhoid, and 2 of relapsing fever. Only one of the typhus cases had no local or general reaction, as claimed by Friedberger, and the other four had a definite local reaction, while the constitutional disturbance was only a little less pronounced than in the typhoid cases. A local and general reaction was constant in all the typhoid cases, in some of whom the constitutional disturbance was so violent as to contra-indicate the general employment of the method. The two cases of relapsing fever showed the ordinary local reaction, and one a little cyanosis and coldness of the extremities. Delamare concludes that Friedberger's reaction is far from being vigorously specific, and that no reliance should be placed upon it in a doubtful case.

During his imprisonment in Siberia, Bauer, of the Second Medical Clinic of Vienna University, made a systematic examination of the Wassermann reaction in 50 cases of typhus in whom there was no history of syphilis, and found that 46, or 92 per cent., were strongly positive. Of the four negative cases two specimens were taken from patients shortly before death, one on the sixth and the other on the twentieth day of disease. When possible the blood was examined again in convalescence, usually between the second and fourth week, with the result that 20 out of 21 gave a negative reaction. The positive case was suffering from pneumonia at the time the blood was taken. Bauer concludes that the Wassermann reaction in typhus is almost always positive if the blood is examined before the crisis, and becomes negative again in convalescence. In doubtful cases, when the Weil-Felix reaction is not available and there is a question of diagnosis between typhus and typhoid fever, a positive Wassermann reaction is in favour of typhus, Bauer having found that the reaction was always negative in typhoid and paratyphoid.

Tushinsky (quoted by Hoare) tested the Wassermann reaction in 142 cases of typhus and obtained a positive result in 55 per cent. The reaction was most marked at the crisis and in cases with severe cerebral symptoms. In the latter a positive result was obtained in 33 per cent. when the reaction was performed with undiluted cerebrospinal fluid.

In addition to the eruption, Turcan attaches considerable diagnostic value to the insomnia of typhus, which is complete and refractory to any treatment, the blackish-brown coating of the mouth and tongue, and the quiet delirium which is of a professional type. Each of these symptoms may be more or less marked, but it is rare for one of them to be entirely absent, except in extremely mild cases, which are hardly ever seen except in countries where the disease is endemic.

Delamare (2) remarks that branny desquamation in typhus, though minutely described by Brauer and Zlatogaroff, has been ignored by numerous writers. It does not appear to bear any relation to the intensity of the eruption, for it was observed fairly often at the end of the epidemic in 1920 and 1921 among the Russian refugees at Constantinople, in whom the rash was very slight and inconstant. The desquamation may occur on the tenth day, but its usual time for appearance is from the twelfth to sixteenth day when the temperature is falling. Sometimes it is not seen until convalescence. It is often confined to the abdomen or thorax, but it may affect the limbs and face, where it is very ill-marked. It is of no prognostic value, since it may occur in fatal cases, but it may be of help in the retrospective diagnosis of typhus when the Weil-Felix reaction cannot be carried out or is doubtful.

In a paper based on the study of about a thousand cases treated in 1919–20, Finkelstein, of Kovno, regards an early change in the heart-sounds consisting in indistinctness, especially at the apex, and a considerable but transient drop of temperature on the morning of the third day as of value in the early diagnosis of typhus.

According to Cheinisse, Vinokouroff, of Odessa, regards punctiform haemorrhages in the uvula as an early and constant sign of typhus in children. The only other two diseases in which these haemorrhages in the uvula are present, viz. scarlet fever and whooping-cough, are not likely to be mistaken for typhus. Vinokouroff's sign appears at the same time as the respiratory catarrh and even in its absence during the first two days of the disease, and becomes very pronounced on the third day, but begins to fade as the characteristic eruption develops, and completely disappears by the end of the first week.

Prophylaxis. Mitchell and Richardson describe the prophylactic measures employed in the British Military Mission to Denikin's army during the winter epidemics of 1918–19 and 1919–20. In addition to general measures, such as closely cropping the hair of all patients on admission to hospital, bathing and spraying them with methylated spirit, and putting them into entirely fresh clothing before taking them into the ward, specific prophylaxis was attempted by means of a vaccine which consisted of sterile typhus blood free from fibrin, taken from a patient without any other disease on the first to third day of the rash. Three doses of this vaccine were given in the arm subcutaneously or intramuscularly at intervals of five to seven days, the amounts being 1 c.cm., 2 c.cm., and 2 c.cm. No general reaction was observed. Of 195 members of the mission who had been freely inoculated in this way only one, or 0·5 per cent., subsequently developed typhus, whereas out of 800 who were not inoculated at all or not fully inoculated 89, or 11 per cent., contracted the disease. The writers conclude that though these results are suggestive the prophylaxis of typhus by inoculation has not yet been placed on a firm basis.

Treatment. Hausmann, of Moscow, recommends the substitution of sedative treatment for stimulation in typhus on the following grounds: (1) The deleterious effects of sleepless nights on the general condition, especially the heart and vessels, and the beneficial effect of artificially produced sleep; (2) the fact that persons with healthy circulatory organs not infrequently succumb, while others with a severely damaged heart often survive; (3) the fact that typhus patients often present a high degree of hyperpnoea (40–60 respirations in the minute) which cannot be explained by the temperature or the condition of the heart and lungs; (4) the fact that after long persistence of hyperpnoea the respiration ceases, while the heart still continues to beat. The aim of sedative treatment is to: (1) diminish the toxaemic excitability of the respiratory centre; (2) to inhibit reflex action on this centre; (3) to remove all psychical and somatic stimuli. Hausmann accordingly from the beginning of the disease gives bromide to his typhus patients, subsequently combining it with small doses of morphia in an infusion of convallaria majalis, a drug which in addition to its cardiac action has an undoubtedly sedative effect. Sleep must be obtained at all costs. If bromides are ineffectual, one of the fatty acid series, such as veronal, luminal, medinal, or adalin, combined with morphia, should be tried. Pain of any kind, particularly headache, must be combated by analgesics, especially pyramidon. The bowels must be kept open regularly, as constipation irritates the respiratory centre as well as having an injurious effect on the general condition.

Retchmensky (quoted by Cheinisse) advocates an abortive treatment consisting in mercurial injections (cyanide or salicylate of mercury in doses of 0·007–0·008 gm. daily). From his experience of this method in 51 cases he has come to the conclusion that if employed during the first four days it can cut short the disease, whereas if used later its action is doubtful or nil.

During the great Roumanian epidemic of typhus, which occurred in the winter of 1916–17 and the following spring (see *Medical Science*, 1920, **1,** 561), Savini, of the Jassy Faculty of Medicine, treated 24 cases between the fifth and tenth day of disease with a vaccine consisting of a mixture of blood and cerebrospinal fluid obtained from patients during the first six days of the disease. The effect of the treatment was to cause a disappearance of the symptoms, produce a premature defervescence by lysis, and shorten the period of convalescence, no complications being observed in the cases treated by the vaccine. In addition to the 24 patients on whom the vaccine had a beneficial effect, there were 18 on whom it had little or none because it was employed too late. In ordinary cases the method of treatment was as follows: on the first day an injection of 5 c.cm. of the vaccine heated to 55° C. for 15 minutes was given in the morning and 10 c.cm. in the evening. On the second day 5 c.cm. of vaccine heated to 50° C. for an hour was given in the morning, followed by 10 c.cm. in the evening. On the morning of the third day an injection of 5 c.cm. of vaccine heated to 50° C. for half an hour was given in the morning and 10 c.cm. in the evening. The doses of the subsequent injections were 10 c.cm. morning and evening until the temperature became completely normal.

Benhamou, Jahier, and Barthélemy found that the best results were obtained by intravenous injection every two or three days of a convalescent's whole blood, 100 to 200 c.cm. of the donor's blood being received into a 10 per cent. solution of sodium citrate.

Brenner, of Lemberg, treated about 150 cases of typhus in the course of the year with turpentine or its derivative terpene hydrate. He first gave it by mouth in the form of pills and alcoholic solution, or by rectum in suppositories, but subsequently found it more effective when given by inhalation, small plugs of cotton-wool moistened with turpentine oil being inserted into the nostrils and changed at frequent intervals according to the intensity of the symptoms. When this treatment was started early, i. e. between the third and fifth day of disease, it shortened the disease and caused a rapid fall of temperature. In a large number of cases it had a favourable effect on the subjective symptoms, especially headache and insomnia, as well as the objective symptoms, especially motor restlessness and tremor. Bronchial symptoms did not develop or only in a moderate degree, and the drug had a favourable action on the heart and circulation.

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DISEASES OF THE SPLEEN

Thrombosis of the splenic vein. According to Bais, who records a case in an anaemic woman in whom thrombosis of the splenic vein was rapidly followed by portal thrombosis with subsequent infarction of a large part of the jejunum and ileum, 32 cases of infarction of the entire spleen were collected in 1918 by Nuzum, including four of his own. In only seven of these cases, however, was the cause of the infarction thrombosis of the splenic vein; in all the others the cause was obstruction of the splenic artery or vein by malignant growth, embolism of the splenic artery, or torsion of the pedicle of a wandering spleen. Little is to be said with regard to the symptoms of splenic infarction, but pronounced tenderness and pain in an enlarged spleen are suggestive. Some cases have been described by Ewald in which fatal haematemesis has occurred. In Bais's case the enlarged vessels on the stomach wall indicated the possibility of this occurrence.

Frick, of Chicago, who records an illustrative case, points out that in the presence of chronic splenomegaly with attacks of recurrent gastrorrhagia, and in the absence of other symptoms of portal thrombosis, especially haemorrhoids, chronic diarrhoea, ascites, caput Medusae, and intestinal haemorrhage, a diagnosis of thrombosis of the distal portion of the splenic vein is justified and splenectomy is clearly indicated. It should be performed preferably at an opportune time, but is indicated also as an emergency measure during an attack of gastrorrhagia if it can be done immediately after a blood transfusion. Frick's patient was a man, aged 61, in whom chronic splenomegaly was accompanied by attacks of gastrorrhagia due to recurrent thrombosis of the splenic vein. An *ante mortem* diagnosis of portal thrombosis of eighteen years' standing was made. The autopsy showed that the splenomegaly, and particularly the gastrorrhagia, were due to obstruction not in the portal but in the splenic vein.

Ogilvie reports a case of spontaneous rupture of the splenic vein in a man aged 31, with an enlarged liver and spleen, who had had attacks of jaundice every two or three months for the last eight or nine years. Splenectomy was performed, but death took place a few hours later. At the autopsy the spleen was found to be fibrotic and to weigh 640 gm. The liver showed cirrhosis, on which was implanted a primary hepatic carcinoma with large hepatic cells arranged in irregular nodules.

Aneurysm of the splenic artery. According to Garland, of Boston, who reports an illustrative case, aneurysm of the splenic artery has been found only three times in over 4,100 autopsies performed at the Massachusetts

General Hospital. Garland has collected seventeen cases from the literature, the most recent of which, recorded by Högler in 1920, was diagnosed during life. His own case occurred in a man aged 52, in whom the aneurysm ruptured on paracentesis abdominis for ascites, death occurring 3½ hours after the operation. The rupture may have been due to the excitement caused by moving the patient and performing the tap, or a withdrawal of a litre of fluid from the abdomen may have caused a relative drop in the pressure of the structures surrounding the aneurysm. The autopsy showed that the rupture was not due to direct trauma by the trocar.

Splenic anaemia. Hallez has collected 124 cases of splenic anaemia or pseudo-leukaemic anaemia. All but four, aged from two to five years, were less than two years of age, and almost all were between six and twenty months. When a severe anaemia occurs after the age of two years, it very rarely gives rise to splenomegaly, only a few cases of pseudo-leukaemic anaemia having been recorded in the adult (Strümpell, Vaquez and Aubertin, Minet, Paisseau, and Lemaire). Numerous aetiological factors have been incriminated, and have been classified as follows in the present series: syphilis in the infant or its parents, 47 cases; tuberculosis in the infant or its parents, 11 cases; rickets without obvious syphilis or tuberculosis, 27 cases; digestive disorders, errors in diet, 15 cases; malaria, 7 cases; unknown causes, 17 cases. The onset of the disease is almost always insidious, and it is only after some weeks, and sometimes months, that the infant's condition gives rise to uneasiness. The duration of the disease is often shortened by complications, such as broncho-pneumonia, choleriform diarrhoea, less frequently miliary tuberculosis, haemorrhages, or infective purpura. The prognosis is therefore very grave, but not invariably fatal, especially if the cause has been recognized and removed. Hallez maintains that pseudo-leukaemic infantile anaemia is not a distinct affection but a syndrome representing the highest degree of anaemia in infancy with an undoubted relationship to other haematological conditions. He is of opinion that it may be transformed into leukaemia, just as a benign growth may be converted into a malignant tumour. It is not necessarily, however, the initial stage of leukaemia, as some writers, such as Martelli, maintain.

De Stefano has observed 23 cases of splenic anaemia in children aged from 12 months to 9 years at the Naples University Institute of Clinical Paediatrics, in almost all of whom the presence of syphilis or tuberculosis or of both infections combined could be established in the child or the parents. Syphilis alone was found in 13, and in association with tuberculosis in 6, while tuberculosis alone was present in 2. In only two instances was it impossible to discover any evidence of either disease. De Stefano comes to the conclusion that apart from cases of direct transmission of syphilitic or tuberculous infection from the parents to the child with localization of the infection in the haemopoietic organs, splenic anaemia may be regarded as an inherited dystrophy of the haemopoietic system, on which any morbid factor may act as an occasional cause.

In a study of infantile splenic anaemia Evans and Happ, of the Johns Hopkins Hospital, came to the following conclusions: (1) In infants with anaemia enlargement of the spleen is frequent and enlargement of the liver and lymph nodes is fairly common. These findings alone are of no specific diagnostic or prognostic importance. (2) The infantile haematopoietic system frequently reacts to anaemia with a relative lymphocytosis, by throwing out immature blood-cells, or with both these qualitative changes, in varying degrees of severity. Any of these reactions may be present with or without leucocytosis and have no serious significance. (3) The presence, absence, or degree of splenomegaly, hepatomegaly, or general enlargement of the lymph nodes, the severity of the anaemia, the total white blood-cell count, or the type of qualitative changes in the blood bear no constant relation to each other. (4) This symptom-complex has not been shown to be a disease *sui generis*, and all variations of it are merely an infantile response to some agent producing secondary anaemia. It is not yet entitled to any name, especially one that suggests a relationship to leukaemia.

Miller reports a case of splenic anaemia resembling von Jaksch's disease in a male infant aged 6 weeks, the youngest case hitherto recorded. Rickets and syphilis could be excluded as aetiological factors. Increase of haemoglobin and the number of red cells with disappearance of the marrow cells from the blood-stream and a gain in weight followed repeated transfusions of small amounts of citrated blood and intramuscular administration of the green citrate of iron (gr. $\frac{3}{8}$ twice a week) together with complementary feedings.

Osman, who gives a summary of 26 cases of splenic anaemia, treated in Guy's Hospital since 1899, comes to the following conclusions: (1) Splenic anaemia is not a specific disease but a clinical syndrome produced by a variety of causes. (2) The syndrome is probably only the result of a chronic infection situated within the spleen itself. (3) In some cases a primary focus of infection can be discovered elsewhere in the body, e. g. in the teeth, tonsils, or uterus. (4) All cases are not necessarily fatal. In some the process is self-limited, and spontaneous cure results.

Although the great majority of cases of Banti's disease on record have occurred in persons above the age of 17 or 18, Canelli, of the Turin University Paediatric Clinic, has collected 31 cases in children from the literature of the last twenty years. Nine were in patients aged from nine weeks to six years, ten from seven weeks to fourteen years, and twelve from fifteen to seventeen. The course of the disease was relatively rapid compared with that seen in the adult, so that it was not always possible to distinguish the anaemic, intermediate, and ascitic stages. The duration of the disease in the 31 cases ranged from four months to twelve years. Haemorrhages were noted in twelve cases, haematemesis and melaena being the most frequent, and epistaxis and gingival haemorrhages coming next. In twelve cases splenectomy was performed; nine recovered or were improved and three died. Of the 31 cases 13 died, 12 recovered, and in 6 the issue was not recorded. As regards the aetiology, although alcoholism, malaria, tuberculosis, syphilis, and rickets do not possess the value of specific predisposing cause of Banti's disease, Canelli thinks that they make the individual more susceptible to it, as they do to other diseases.

De Léobardy, in his Paris thesis, describes two fatal cases, in men aged 51 and 40 respectively, of primary splenomegaly, probably belonging to the type of Banti's disease, and characterized by haematemesis in one case and repeated vomiting and asthenia in the other. In neither case is any mention made of thrombosis of the splenic vein which was found in Frick's patient (*vide supra*). De Léobardy points out that splenectomy in such cases is likely to lead to a permanent recovery and should be chosen in preference to treatment by radium or X-rays.

Splenic abscess. During the last two years Wallace has seen 49 cases of splenic abscess in natives of Northern Rhodesia: 19 were operated on; in the other 30 the condition was not discovered until the autopsy. The causation was obscure. Three cases occurred in women. Children were not affected. Wallace is inclined to regard the condition as a manifestation of influenza which is endemic in Northern Rhodesia, influenza causing thrombosis in the spleen with subsequent softening and invasion of gas-forming organisms from the intestine.

Gaucher's disease. According to Levy, of New Haven, Conn., many cases erroneously called Gaucher's splenomegaly have crept into the literature and have been disproved by careful examination of the clinical data or re-examination of the slides of splenic tissue. Levy states that the absolutely proved cases reported to March 1919 number 21, and that since then no new cases have appeared in the literature. He now reports the twenty-second case in a woman aged 34, who died of tetanus nine days after splenectomy. The spleen weighed only 950 gm., whereas in 13 cases analysed by Brill and Mandlebaum the average weight was 3,600 gm. There was no enlargement of the liver or conjunctival thickening, but otherwise the case presented all the features of Gaucher's disease, including absence of anaemia, jaundice, and ascites. There were bleeding from the nose and gums, absence of enlarged lymph glands, and a persistent leucopenia. Histological examination of the spleen showed a similar structure to that found in cases described as Gaucher's disease.

Mills, Asnis, and Babcock, of Philadelphia, report a case of splenomegaly in a boy aged 3, who presented the following symptoms of Gaucher's disease: (1) insidious onset; (2) the usual age; (3) enlargement of liver and spleen; (4) yellowish-brown discoloration of the skin; (5) numerous ecchymoses; (6) marked perspiration; (7) little if any ascites. On the other hand, there was an absence of the following symptoms, said by Mandlebaum and Brill to be usually present: (1) female sex; (2) familial occurrence; brownish-yellow wedge-shaped thickening of conjunctivae; (4) bleeding from mucous surfaces. The leucocytes numbered 8,400 and the red cells 2,112,000. Splenectomy was performed, and a spleen weighing 4¾ lb. was removed. Sections of the spleen were examined by Mandlebaum, who stated that, in his opinion, it was not Gaucher's disease but some form of leukaemic splenomegaly. The writers discuss the value of splenectomy in promoting longevity in Gaucher's disease, and conclude that if the average duration of life in this disease is 19 years, the argument for early operation loses much of its force. The immediate operation mortality is probably not less than 15 per cent., and it is questionable if in view of this surgical risk much is gained by the operation. In the present case the abdominal distension, associated dyspnoea, and evident progress towards a fatal issue were strong factors in determining operation.

Gerstl, of the German University Children's Clinic of Prague, records a case of secondary dwarfism in a premature infant aged 1 year, caused by (*a*) a form of rickets characteristic of premature births, (*b*) chronic digestive disturbance, and (*c*) splenomegaly of the Gaucher type. Some endocrine disturbance was probably also a contributing factor. Gerstl points out that Gaucher's splenomegaly may occur in an isolated form in young children instead of attacking several members of the same family, and may take an acute course, as in his own case, and one reported by Niemann.

Tuberculosis of the spleen. Bufalini, assistant at the Pisa University Medical Clinic, states that according to Banti's classification three different forms of primary tuberculosis splenomegaly can be distinguished, viz.

(1) caseous tuberculous splenomegaly, (2) splenomegaly with miliary tuberculosis, (3) tuberculous splenomegaly with necrosis. Of these the caseous form is certainly the most frequent, while the miliary form, of which Bufalini records an example, is the rarest. The patient was a woman aged 37, in whom the spleen was removed by Taddei in the belief that the splenomegaly was due to Banti's disease. The patient recovered from the operation, but a year later developed tuberculous cervical adenitis which was cured by iodine, heliotherapy, and periodical evacuation of the abscesses.

Syphilis of the spleen. According to Furno, who records several examples, syphilis of the spleen is not a very rare clinical or anatomical occurrence. It may develop in all stages of the disease and at any age, and seems to be commoner in the female sex. In the secondary stage it appears in the form of a splenic tumour of varying size, and is often associated with haemolytic jaundice which runs a favourable course. In the tertiary stage it may assume a variety of clinical forms, which in order of frequency are splenic tumour with simple anaemia; Banti's syndrome, haemolytic splenomegaly, or haemolytic icterus, and splenomegalic pseudo-pernicious anaemia of the Strümpell type. It is frequently met with in the early or late stage of inherited syphilis, in which it may be manifested by a splenic tumour alone (the commonest form), or by Banti's syndrome, or by haemolytic icterus of the Minkowski-Chauffard type. As a general rule, specific treatment when started early produces a cure, but in some cases it may be ineffective, and splenectomy may be required.

Carcinoma of the spleen. The comparative immunity of the spleen from secondary carcinomatous growths is shown by the fact that Adler in 374 cases of primary carcinoma of the lung found metastases in the liver in 103 cases, in the kidneys in 58, and in the brain in 53, while the spleen was involved in only 18 instances. Sappington, of Philadelphia, who records a case of carcinoma of the spleen in a woman aged 42, secondary to cancer of the breast and part of a general microscopical carcinomatosis, remarks that while carcinoma of the spleen is undoubtedly rare, most of the evidence on which this conclusion is based has been obtained from naked-eye observation only. He suggests that microscopical examination may add considerably to the number of reported cases. In his own case, abdominal massage which had been recommended by an osteopath was probably an aetiological factor.

Cysts. According to Lubbers and Noordenbos, of Amsterdam, who record a fatal case of hydatid disease of the spleen in a man aged 26, only two previous cases of splenic cysts have been recorded in Dutch literature, one of which was due to hydatid disease, while the nature of the other was not established. It is estimated that the spleen is involved in 3·35 per cent. of all cases of hydatid disease. The parasite may develop centrally, as in the writers' case, or peripherally, the splenic tumour forming a thin covering to the cyst. According to Trinkler, central development is the commonest. In hydatid disease of the spleen adhesion of the cyst to the surrounding tissues occurs early, especially when the cyst is large. There are no clinical features to distinguish parasitic from non-parasitic cysts of the spleen. The symptoms are chiefly due to pressure caused by increase in size of the cyst. Hydatid thrill is only rarely found in hydatid diseases of the spleen, and was not detected in the present case. The prognosis depends upon whether the spleen is the only localization of the echinococcus or whether the parasite has invaded other organs as well, general echinococcus infection being an extremely dangerous condition. Even when confined to the spleen echinococcus disease does not offer such a favourable prognosis as non-parasitic cysts of the spleen. In rare instances a spontaneous recovery may occur through rupture of the cysts into the alimentary canal or through death and calcification of the parasites. The best mode of treatment consists in marsupialization or splenectomy.

The difficulty in diagnosing a cyst of the spleen is illustrated by the cases reported by Bevers in a woman aged 44, in whom an abdominal tumour diagnosed as hydronephrosis by Osler was found at the operation to be a splenic blood-cyst, probably the result of infarction.

Various forms of splenomegaly. Aubertin and Giroux report a case which raises the same questions as those of Tuohy and Giffin (vide *Medical Science*, 1921, **4**, 121–2), but are able to reach no definite conclusion. They report the case of Stillman but not that of Tuohy. Their case is as follows: the patient was a male suffering from congenital heart disease and was under intermittent observation for four years. During this time he had several attacks of heart failure and finally succumbed. In addition to symptoms which might be legitimately credited to his cardiac condition, he presented a very marked eosinophilia and slight splenomegaly. The total number of leucocytes varied from normal to 26,000 and later to 30,000. Of these 65–70 per cent. were eosinophils, and these high figures were verified on several occasions. There were some eosinophil myelocytes, but less than 1 per cent. The red cells were slightly diminished. No mention is made of abnormal cells other than the eosinophils, or of the haemoglobin value. Autopsy was permitted, but no microscopic examination could be made. Aubertin and Giroux summarize the features of three cases known to them and come to the following conclusions: the case of Tuohy falls in with the others. The characteristic clinical features are three: (1) persistent eosinophilia with normal adult eosinophils preponderating and practically no abnormalities of other cells, (2) some increase in size of the spleen and glands, the latter perhaps only appreciable at autopsy, and (3) a very slow evolution. No evidence has been found in any case of such aetiological agents as are known to produce eosinophilia. Giffin's case came to autopsy and an examination showed myeloid metaplasia of the spleen and great excess of eosinophil myelocytes in the marrow. They find few analogies with leukaemia, chiefly on the grounds that the blood shows a very high percentage of myelocytes in the latter disease and because it is of speedier development. It must be admitted that neither of these objections touches the underlying pathology of the disease, however much the clinical picture may be affected, but no one can dispute the authors' conclusion that 'massive eosinophilia', the name they choose, must at present be considered a definite syndrome without clear analogies with any hitherto recognized disease.

Symmers brings forward as a new syndrome telangiectatic splenomegaly. His own case was that of a man of 70 who died very soon after admission to hospital, and he cites somewhat similar cases recorded by Borissowa in a woman aged 52, and by Pentmann in a woman of 56. Borissowa's case has often been discussed in the literature of Gaucher's splenomegaly. These three patients were clinically examples of 'splenic anaemia', but on more detailed examination evidence was found that characteristic lesions were present in other parts of the haemopoietic system, i.e. that these cases formed a group in the large class of generalized reactions of lymphoid tissue.

In Symmers's case lesions were found in the spleen, kidney, lymph nodes, liver, marrow, and skin; in Borissowa's case, in the liver, spleen, and marrow; and in Pentmann's case, in the liver, spleen, and marrow.

The basis of the typical lesion appears to be a proliferation of cells of endothelial type. This is true also of Hodgkin's disease and Gaucher's splenomegaly, both which stand in close relation to Symmers's case. But whereas in Hodgkin's disease these cells are or become fibroblasts, and in Gaucher's splenomegaly undergo a characteristic degeneration, in the cases now described there was evidence of their retaining the power to develop into angioblasts and form new vessels. In Borissowa's case no actual capillaries were formed, in Pentmann's case there were capillaries but no telangiectases, while in Symmers's case the latter were a prominent feature. The name proposed by Symmers is therefore likely to attract attention to a non-essential feature of the disease, and we think that 'Borissowa's disease' would be a better label until such time as an agreed nomenclature based on accurate knowledge of the pathology can be arrived at.

Further, the suggestion implied by Symmers, that the existence of lesions outside the bounds of what is ordinarily regarded as haemopoietic tissue is in some way surprising, accords ill with the fact that such lesions are a frequent feature of diseases with which he considers telangiectatic splenomegaly stands in close relation, viz. Hodgkin's disease, mycosis fungoides, Cohnheim's pseudo-leukaemia, Sternberg's leukosarcoma, and Gaucher's splenomegaly.

There is of late years abundant evidence that all these diseases and leukaemia also must be regarded as generalized reactions of mesoblastic tissue, taking different forms according to the direction of development of the primitive connective tissue-cells, and predominating in one part of the body or another according to laws of which we are still almost completely ignorant.

Wade, chief of the Department of Pathology and Bacteriology of the College of Medicine and Surgery of the University of the Philippines, reports a fatal case, in a man aged 43, of haemopoietic splenomegaly with marrow sclerosis. The disease was of at least two years' duration. The Wassermann reaction was negative, and no malarial parasites were found in the blood. Death took place four days after splenectomy. Examination of the spleen, which weighed 1,775 gm. and measured 25 cm. long by 17 cm. wide, showed very active haemopoiesis with here and there discrete nodules of marrow-like tissue wholly foreign to splenic structure. There was a complete lack of haemopoietic activity in the bone-marrow, much of which had undergone marked osteofibrosis. Some haemopoietic activity was found in the liver and prevertebral lymph glands. The causation of the condition was quite obscure. Wade considers that the case was an example of the rare group in which the bone-marrow is the seat of marked sclerosis and is incapable of producing blood-cells, at least in the needed amounts. There was not much anaemia owing to the spleen having assumed a very active erythrogenic function, incidental to which almost tumour-like nodules of pure marrow-like tissue developed throughout the organ.

Hutcheson, of Richmond, Va., reports a case in a woman, aged 35, who had clinically many of the features of hypertrophic biliary cirrhosis, viz. jaundice, enlarged liver and spleen, fever, pain, and clubbed fingers. Portal obstruction, however, occurred early. At the autopsy the liver weighed 2,394 gm. and contained numerous abscesses filled with greenish pus, from which a Gram-positive diplococcus of the pneumococcus group was grown.

The spleen weighed 1,888 gm., and was smooth and rather soft. It showed no gross or microscopical abscesses and no evidence of thrombosis. The microscopical appearance was that of an acute splenic tumour such as is found in the septicaemias.

Gibson details a certain number of diseases in which, in spite of varying clinical characteristics, the splenic condition is of the same type and is characterized by congestion or stasis, haemorrhage, endothelial proliferation, sclerotic lesions of the vessels, endophlebitis of pulp veins, infarcts, a tendency to amyloid change, and embolism of the splenic vein. The usual clinical symptoms presumed to result directly from the splenic inflammation are local pain, anorexia with or without fever, retardation of growth, anaemia, rarely polycythaemia, varying types of white-cell reaction, hepatic inflammation, and haematemesis.

Gibson then deals in detail with certain cases in which the nature of the infection is known, namely, syphilis, tuberculosis, acholuric jaundice (known to be due to varying organisms in its acquired form), and splenic anaemia. With regard to the latter, it is evident that Gibson expects that we shall in due course discover a bacterial cause, presumably resident in the spleen itself and exercising its malign influence from that focus. In a few cases the writer has discovered organisms that may have been aetiological.

Diagnosis. Wohlgemuth remarks that many writers have recommended diagnostic puncture through the abdominal wall in various disorders of the spleen, such as hydatid disease, abscesses, cysts, and tumours. Some authorities have drawn attention to the danger of the method, but chiefly on account of the possibility of introducing organisms into the abdominal cavity, while the possibility of fatal haemorrhage has received little attention. Wohlgemuth reports a case in which, owing to the probability of a subphrenic abscess, an exploratory puncture was made below the left costal arch. No pus was found, but only blood containing haemolytic streptococci. Death took place 10 hours later. The autopsy showed 2,500 c.cm. of partly clotted and partly fluid blood in the abdominal cavity and three punctures in the spleen. Numerous small abscesses were found in the left kidney.

Splenectomy. The indications for splenectomy are discussed by Morawitz, director of the Würzburg Medical Clinic, who remarks that the pathology of the spleen during the last 10 years has become the subject of medico-chirurgical interest. Apart from purely surgical diseases, Morawitz regards the operation as indicated in those conditions in which there is an abnormal haemolysis, when there is reason for supposing that this is taking place in the spleen. This condition is best exemplified in chronic haemolytic jaundice, for which Banti was the first to recommend splenectomy, 21 cases of which were collected by Eylenburg in 1921, though Morawitz considers that the real number is much larger. Although all writers are agreed that the jaundice, anaemia, and subjective symptoms usually completely disappear after the operation, Morawitz does not recommend splenectomy in every case of haemolytic jaundice, but only in those in which the capacity for work or pleasure is much impaired by anaemia and pain in the liver and spleen. The value of the operation in pernicious anaemia is much more questionable. Undoubtedly remissions of considerable duration do occur after splenectomy, but of 16 cases collected by Eylenburg only one was alive at the end of five years. The remissions in Eylenburg's cases were never complete and the red-cell count did not exceed 2½ millions. Owing to the great danger of the operation, from which Eppinger saw four deaths among 18 cases, it should only be recommended when all other methods, including arsenic and transfusion, have been tried in vain, and haemolysis appears to be partly responsible, as shown by enlargement of the spleen. During the last few years splenectomy has been successful in cases of morbus maculosus (Glanzmann) or essential thrombopenia (Frank). In leukaemia and erythraemia not much is to be expected from the operation, though occasionally very long remissions have been reported, e. g. by Toenissen (vide *Medical Science*, 1921, **5**, 12). In hypertrophic cirrhosis of the liver the operation has been followed by disappearance of the jaundice and decrease in size of the liver. Permanent success, however, has not been recorded in this condition, and in Gaucher's disease the results were only transient.

According to Bartlett, of New York, the indications for removal of the spleen depend on certain criteria, not on the making of a definite diagnosis. The criteria are splenomegaly, secondary anaemia, and the failure of repeated blood transfusions to determine an improvement in the anaemia and general blood condition. Before deciding to remove the spleen it is important to exclude leukaemia, in which the operation is contra-indicated. It is desirable to remove the spleen in the early stages of the pathological process for which splenectomy is indicated. Bartlett has collected reports of 51 splenectomies in children under 14, consisting of the following cases: von Jaksch's disease 5, splenic anaemia and Banti's disease 20, Gaucher's disease 4, haemolytic jaundice 15, tuberculosis 1, septic splenomegaly 1, unclassified cases 5.

Mayo's paper is chiefly notable for the figures he gives of splenectomies performed at the Mayo Clinic, i. e. under the best possible conditions. Up to Jan. 1, 1921, 249 spleens had been removed with a mortality of slightly over 10 per cent. Of these, 71 were for idiopathic splenic anaemia with 9 deaths. 11 were removed for chronic sepsis with 3 deaths, and 6 for syphilis with 1 death. 8 children suffering from splenomegaly were operated upon without fatality, and an unstated number of malaria cases which had a high mortality. Mayo points out that the operative risk is greater with every year of duration of the disease, old splenomegalics with adhesions being difficult to remove and these patients least able to bear prolonged operations.

Weinert states that though splenectomy is not prejudicial to the patient it is not correct to state, as several recent writers have done, that the loss of the spleen has no demonstrable influence on the composition of the blood. For a varying period after splenectomy there are lymphocytosis, eosinophilia, and often mononucleosis. The principal change in the red cells is the appearance of Jolly's bodies, i. e. red corpuscles containing the remains of nuclei, which persist in the peripheral blood for years and perhaps throughout life. As a general rule they are more marked after removal of a diseased spleen, as in haemolytic jaundice or splenic anaemia, than after removal of a previously healthy organ for rupture. In recent splenectomies for ruptured spleen in the Magdeburg Surgical Clinic, Weinert has observed a rise in the number of the red cells from 2,200,000 to 3,700,000 and 4,000,000 within a few weeks.

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J. D. R.
G. W.

ABSTRACTS

SURGERY

Anzilotti, G. Osservazioni sulla pseudo-botriomicosi o granuloma peduncu-lato telangectasico. [**Observations on pseudo-bothriomycosis or pedunculated telangiectatic granuloma.**] *Policlin.*, 1922, **30**, Sez. Chir., 301.

A study of fifteen cases of pedunculated granuloma—a small red tumour projecting from the skin, through which it appears to have burst, since the skin-edge makes a collar round the peduncle. The surface bleeds at a touch and is usually covered with inspissated blood and serum. The commonest site is a finger on the palmar aspect, but several have been noted on the face and one on the lateral aspect of the tongue. Where the history is clear, the initial cause seems generally to be a punctnre by a straw-stalk or a splinter of wood, though other similar wounds may be the starting-point. The lesion is slow in developing, and may be of some duration, for the author's cases had been in existence for periods from fourteen days to four months.

The tissue is of granulation type, save that in the deeper layers the numerous vessels are of adult rather than of embryonal form, and constitute a neoplastic rather than inflammatory picture. Only staphylococci have been recovered, and these, upon injection, do not reproduce the lesion; nor indeed does implantation of fragments of the 'growth' itself. No protozoon or sporozoon was demonstrated.

Despite his chosen title the author emphasizes the complete dissimilarity between these lesions and those of bothriomycosis in animals. He refers to, but has not repeated, the experiments of Galli-Valerio, who did produce closely analogous lesions by using strains of staphylococci cultivated on straw. He considers the conditions of vegetative dermatitis and folliculitis, and the 'fungus' nodule seen at the umbilicus, and concludes that whether due to some peculiar property of the strain of organism, or to an accident of site of inoculation in the dermis, or some special quality of the host-tissue, the telangiectatic result is but some modification of tissue-reaction and not a true neoplasm. In any case, complete excision leads rapidly to healing by first intention. E. R. C.

Bertocchi, A. Contributo allo studio dei tumori multipli maligni 'diversi generis'. [**Contribution to the study of multiple malignant tumours of different types.**] *Policlin.*, 1922, **30,** Sez. Chir., 361.

The author had a patient who suffered simultaneously from an angio-sarcoma of the thigh and an epithelioma of the face. His contribution consists mainly of a collection of cases from the literature, which is not, however, by any means complete. He regards the occurrence of multiple primary malignant tumours as of great rarity, and finds that all theories attempting to explain the phenomenon hark back to theories of the origin of tumours, of which none so far obtains general acceptance. Whilst some authors consider the matter one of pure chance, others think that the presence of one tumour definitely favours the growth of another, and he advances the work of Centanni upon the action exerted by special diet on the survival and growth of experimental tumours, together with that of Freund and Kaminer upon the protective action of blood-serum of the cancerous on carcinoma cells, as suggesting the existence of a general state of the organism favouring the appearance and growth of tumours, more especially in those already the hosts of one malignant neoplasm.

E. R. C.

Lee, Burton J., and **Adair, Frank E.** (1). **Traumatic fat necrosis of the female breast and its differentiation from carcinoma.** *Ann. Surg.*, 1920, **72**, 188–95.

Lee, Burton J., and **Adair, Frank E.** (2). **Traumatic fat necrosis of the female breast and its differentiation from carcinoma.** *Surg. Gynec. & Obst.*, 1922, **34**, 521–31.

In these two papers Lee and Adair set forth the clinical, operative, and pathological findings of five cases of this hitherto undescribed condition. In the first paper two cases are recorded, and in the second three more of their own are recorded, and two cases verbally reported to them by Bloodgood are also mentioned.

The simulation of carcinoma is very close, both clinically and, at first sight, pathologically. In each case there had been a definite precedent trauma of the breast in the definite locality in which the tumour afterwards arose; in the third case, however, the recorded trauma occurred ten years, and in the fifth case eight years, before the patient was operated upon for the fat necrosis. The pathological anatomy has been worked out by Ewing, the well-known New York tumour pathologist.

The clinical manifestations may be rapidly summarized by the table extracted from the second paper.

Case.	Age.	Weight.	Trauma.	Pain.	Tumour hardness.	Breast corpulent.	Nipple retraction.	Skin fixation.	Deep attachment.	Axillary nodes.	Supraclavicular nodes.	History of visible haemorrhage.	Patient noted duration.	Pre-operative diagnosis.
1	52	190	Blow on breast 3 mths.	0	X	X	0	X	X	0	0	0	3 mths.	CA
2	36	211	Hypodermoclysis 7 mths.	0	X	X	0	X	0	X soft	0	0	7 mths.	CA
3	40	191	Hypodermoclysis 10 yrs.	0	X	X	0	0	X	0	0	0	1 mth.	Benign tumour
4	47	152	Hypodermoclysis 10 mths.	X	X	X	X	X	0	0	0	X	10 mths.	Traum. fat necrosis
5	54	180	Fell 13 steps striking post 8 yrs.	X	X	X	0	X ?	0	0	0	X	3 wks.	Fibroadenoma

Pathological examination showed the following:

Case 1. *Gross examination:* tumour mass in the breast 2 cm. in diameter, irregular, circumscribed, but not encapsuled. It merged along one border into the fatty tissue and elsewhere into the breast tissue; it was opaque, brownish yellow, and lacked definite cicatricial character and chalky streaks. The whole breast was uniformly fibrosed and contained no cysts. Axillary nodes slightly enlarged and not carcinomatous (they were not palpable clinically). *Microscopic examination:* broad areas of fat necrosis surrounded by a broad zone of new cellular tissue containing large vessels which showed active endarteritis obliterans. In places in the necrotic areas there was connective tissue containing several large giant cells. No spirochaetes were found in the tissues.

Case 2. *Gross examination:* indurated area 2 × 1 × 4 cm. slightly cicatrized, not quite hard enough for carcinoma; well circumscribed, also entirely encapsulated, apparently a fat lobule which suggested a tumour process. On section it was opaque and light yellow, not translucent, and without definite chalky or silvery points. In the neighbourhood of a smaller fat lobule there were a few similar slightly opaque points. Also in the neighbourhood was a cyst 1 cm. wide with a blood-stained wall and creamy contents. The remainder of the breast was normal. *Microscopic examination:* a chronic productive inflammation in fatty tissue; no evidence of carcinoma; fat cells were prolific, and many small giant cells were present. Much diffuse new fibrous tissue; in places were collections of lymphocytes and occasionally a few cysts. The large cyst was lined with large epithelial cells of the sweat gland type.

Case 3. *Gross examination:* the excised tumour was 3 cm. wide, and presented a cyst with whitish hyaline capsules 1 mm. thick and yellow granular semi-fluid contents. Outside one half of the periphery of the cast the fat tissue appeared necrotic over an irregular area 1 cm. to 2 cm. wide. *Microscopic examination:* thick laminated hyaline connective tissue-wall around the softening cavity, which contained necrotic fatty material. In the breast outside this wall there was active productive inflammation and many round cells about the ducts and the breast, foci of lymphocytes, and new connective tissue.

Case 4. *Gross examination:* chronic productive inflammation with much new fibrous tissue, minute cavities, and streaks of opaque fatty tissue in an area of the breast measuring 4 × 5 cm. *Microscopic examination:* new acellular connective tissue, small foci of fluid fat surrounded by giant cells, foci of necrotic or structureless fat and islands of normal gland tissue.

Case 5. *Gross and microscopic examination:* chronic productive inflammation in the fat tissue, small central cavity filled with semi-fluid, fatty material, about which were many similar small cavities, around which giant cells were forming.

In paper II, the authors publish numerous illustrations showing the microscopic appearances and some of the clinical features. The attachments to the skin and, in some of the cases, to the deeper fasciae are clinically very suggestive of carcinoma. The authors believe that traumatic fat necrosis of the breast is a definite clinical entity, that it is benign, and that clinically it more closely resembles carcinoma of the breast than any other condition. They state that a distinct history of trauma to the breast and a well-circumscribed firm mass, unassociated with pain or with firm axillary nodes, suggest the possibility of fat necrosis. It is remarkable that this condition has not been recognized by others, but in view of the clear description given by Lee and Adair, and of the associated statements by Ewing and Bloodgood, it is possible that it is more common than is realized. These papers have been abstracted in the hope that surgeons and pathologists will watch carefully for other cases. C. C. C.

Hedblom, C. A. Combined transpleural and transperitoneal resection of the thoracic oesophagus and cardia for carcinoma. *Surg. Gynec. & Obst.*, 1922, **35,** 284–9.

Hedblom reports the case of a man, aged 52, upon whom he performed this operation on May 15, 1922.

The preliminary diagnosis was carcinoma of the oesophagus. Preliminary thoracostomies were performed on April 7, April 11, and April 24 under local anaesthesia and gas-oxygen analgesia; at these operations the 5th to the 11th ribs, inclusive, were resected from the angles to the costal cartilages. On May 15, under local and gas-oxygen anaesthesia, the tumour was removed. The incision began to the left of the middle line, just below the costal margin, and extended outward and upward to the anterior axillary line. The peritoneal cavity was opened, and it was then found that the growth was in the cardia and extended up the oesophagus. The excision was extended up to about the 4th rib in the mid-axillary line and the pleural cavity was opened widely. A considerable quantity of sero-sanguineous fluid escaped and the lung was found partly collapsed. No embarrassment resulted. The diaphragm was split, the pleura over the lower oesophagus incised, the right vagus nerve separated from the oesophagus and the left one cut; the pulse and respiration were unaffected thereby. The lower 4 cm. of the oesophagus, most of the lesser curvature of the stomach, and the upper third of the greater curvature, together with a piece of adherent liver edge, were resected between clamps, with the actual cautery. The stomach was closed by triple suture, and the tube-like cone of stomach stump was stitched to the median angle of the wound. The diaphragm having been sutured, the oesophageal stump was stitched to the skin edge in the mid-axillary line and the rest of the wound was closed. Post-operative blood transfusion and proctolysis were carried out. The growth was of a leathery, annular type without much ulceration of the mucosa. On the third day after operation the oesophageal stump was opened by the removal of crushing clamps which had been left on it at the end of the operation. On the fifth day the tubular end of the stomach was opened and through a catheter food was introduced, presumably into the duodenum. On the fourteenth day a 5-millimetre tube was inserted between the two stomata and allowed swallowing of milk without much leakage. On July 21 the patient had gained several pounds in weight, his haemoglobin had increased from 35 per cent. to 65 per cent., and he was taking all his food, including milk, toast, cereal, and boiled egg, via mouth, oesophagus, and tube.

Hedblom mentions one previous case operated on by this method, by Zaaijer, in 1913. C. C. C.

Moszkowicz, L. Die Dickdarmresektion nach der Vorlagerungsmethode. [**Resection of colon by the Paul-Mikulicz operation.**] *Arch. f. klin. Chir.*, 1921, **160**, 160.

The resection of the colon by the method of Paul and Mikulicz is that in which the loop of gut containing the growth is mobilized and brought out of the abdomen. Later the brought-out loop is cut away and finally the colostomy thus brought about is closed. This method was introduced with a view to minimizing the risk of sepsis within the peritoneal cavity, and Mikulicz brought down his mortality from resection of the colon to 12 per cent. The disadvantages of the method are the length of time required to complete the treatment (six to seven months), the dangers associated with the closure of the artificial anus, more particularly in the crushing of the spur, the frequency of post-operative hernia, and the incomplete removal of the lymphatic drainage area. Moszkowicz claims that his modification of the operation avoids all the disadvantages except the last.

The contra-indication to the operation is the presence of obstruction. If this be present, it must be relieved and nothing more done until the patient's condition has improved, which may mean a delay of one or two months. Moszkowicz reserves the operation for those cases in which the general condition of the patient, apart from the obstruction, is bad.

The first stage of the operation consists in the mobilization of the portion to be removed, and the ligature of the vessels belonging to it. The two ends, proximal and distal, of the loop are approximated and sewn together for a length of 10 cm., the line of suture being on the antimesenteric aspect in order to avoid injury to the mesentery in the subsequent crushing of the spur. The peritoneum is closed and the parietal layer is sewn to the approximated ends of the loop, so that the suture by which they were joined lies outside the peritoneal cavity; the rest of the abdominal wall is now closed above and below the loop. This being completed, the loop containing the growth is removed about 2 cm. from the abdominal wall, the cut ends of the bowel being kept closed by forceps; these forceps are removed in two days' time to allow of the opening of the bowel.

The second stage: six to seven days later the deeper portion of the spur is crushed by Kocher's crushing forceps, the necrosis being hastened by tying a small piece of rubber tube through the hole thus made in the spur. At the end of the second week the necrosed spur has gone, while in three weeks' time the wound should be clean and ready for the final stage of the operation.

The final stage consists in separating the mucous membrane from the skin and the closing of the opening in the bowel by catgut sutures; then the wound is further opened up, a second line of suture applied to the gut, which is then separated from the abdominal wall down to the serous layer, when another suture is applied to the intestine. The abdominal wall is then closed by a few loose sutures with an opening left in the middle for a gauze plug.

Moszkowicz claims to have reduced the time necessary for the method to six weeks. He does not advise it for tumours of the right side of the colon on account of the necessary involvement of the small intestine and the irritation of the skin from the contents of this portion of the gut. He gives details of nine cases, only one of which died as a result of the operation; of the remaining eight, one died of recurrence three years after operation, and the rest were alive 8, 7, 7, 5, 5, 2, 1 years respectively after the operation.

G. E. O. W.

Nielsen, N. A. About the choice between medical and surgical treatment of ulcus ventriculi s. duodeni. [**B.**] *Acta Chir. Scand.*, 1922, **55**, 57.

Nielsen answers the question conveyed in the heading of his paper in an oblique fashion by investigating the possible relationship of malignant disease to ulcer of the stomach and duodenum. His long survey of the subject shows that for several decades the belief has been held that ulcers in these regions predispose to malignant disease. His own investigations suggest the somewhat revolutionary opinion that this teaching is nothing more than a myth. His material consists of the 528 patients treated for gastric or duodenal ulcer in the medical department of the Rigs Hospital in Copenhagen in the period 1897–1915. In 262 cases the subsequent fate of the patients was ascertained 2½–19 years after discharge from hospital. For various reasons 41 cases were withdrawn as being misleading.

In 92 of the remaining 221 cases, gastro-enterostomy, or resection, was subsequently performed, and in most the symptoms disappeared soon after operation, and they persisted for 1 to 8 years after operation only in 20 cases. Of the 221 patients, 44 died after leaving hospital, and 12 contracted gastric cancer, from which 11 had died. A classification of the 221 patients according as their symptoms had lasted less than 6 years, or from 6 to 57 years, showed 66 in the first class, 155 in the second. In this latter class there was only one patient dying from cancer of the stomach. No greater tendency to gastric cancer than exists in the general population could thus be proved among the 155 patients with clinically definite symptoms of active ulcer for 6 to 57 years. In this group there was a second case of cancer, but the patient was still alive after resection of the stomach in 1914. In the second class, represented by 66 patients, there were as many as 10 deaths from cancer of the stomach, and Nielsen argues that these were cases of primary cancer, simulating ulcer closely. 'Of course, this investigation cannot exclude the *possibility* of the origin of carcinoma in a gastric ulcer; but it does not support this possibility.' Hence the conclusion that the possibility of malignant degeneration of an ulcer should not exercise any influence on the treatment of undoubted simple ulcer of the stomach or duodenum.

Seeking to distinguish between the cancer which simulates ulcer and simple ulcer of the stomach, Nielsen has investigated the duration of the symptoms and the age of the 10 cases of carcinoma masquerading as simple ulcers, and he finds that, like other cancers, and in contrast to about two-thirds of all cases of simple ulcer, the ulcer-simulating cancer gives rise to symptoms in the overwhelming majority of cases after the 30th year; the average age of these 10 patients at the first appearance of symptoms was 43·5 years. A study of the literature of *carcinoma ex ulcere* revealed records of 41 cases in which the duration of the symptoms before death was stated exactly. In 22 of these cases it was less than 2 years, and only in 10 did it exceed 6 years. The average age at which the symptoms first appeared in these 41 cases was 45. Hence the conclusion that these cases, like Nielsen's 10, were cases of primary malignant disease and not *carcinoma ex ulcere*. It is evident, therefore, that when symptoms have begun before the 30th year there is little chance of the disease being or becoming malignant. But if the first symptom begins after the 30th year, and the interval between the first symptom and the seeking of medical advice is short, and if symptoms soon recur after medical treatment for ulcer, a cancer simulating an ulcer should be suspected. These considerations and data are often sufficient to distinguish between cancer and simple ulcer, or at any rate to justify operative interference, although none of them draw a sharply distinctive line between the two diseases. C. L.

Metcalfe, R. F., and **Fletcher, L. Z. Ruptured spleen.** *Ann. Surg.*, 1922, **75**, 186.

The authors report three cases of rupture of the spleen, two of which were spontaneous ruptures of normal spleens, malaria and other diseases being carefully eliminated. The third case was traumatic. It is interesting to note that the two spontaneous ruptures occurred apart from any strenuous exercise and simply presented the symptoms of sudden onset of pain in the abdomen followed by collapse. Later there was abdominal tenderness but no rigidity nor distension. The third case was an accident, the patient being thrown from a motor cycle. He also developed collapse, but in addition the abdomen showed board-like rigidity throughout. All three cases were young healthy men and all made good recoveries from operative treatment. The authors lay stress upon the fact that all three patients showed severe pain radiating to the left shoulder, which they regard as a pathognomonic symptom, and which was immediately relieved by operation.

A list of several reported cases of spontaneous ruptures in healthy and diseased spleens follows. A. J. W.

Hurst, A. F., Tanner, A. E., and **Osman, A. A. Addison's disease, with severe anaemia, treated by suprarenal grafting.** *Proc. Roy. Soc. Med.*, 1922, **15** (Clin. Section), 19.

The authors report a case of Addison's disease in which suprarenal grafting caused improvement, at any rate up to the present. During four months of medical treatment, the patient became very anaemic and the systolic blood-pressure fell to 70 m.m. Hg. On March 25, 1921, a suprarenal gland from a man, just dead as the result of accident, was grafted into the subcutaneous tissue of the groin. The blood-pressure remained as before. On April 11, a graft from a foetus just dead was inserted into the substance of the left testicle. A month later blood transfusion was performed. Slow improvement followed. A month later the systolic blood-pressure was 95 m.m. Hg; in February 1922 he had greatly improved; no vomiting for several months. Systolic blood-pressure 115 m.m. Hg; haemoglobin 80 per cent.; spleen still palpable; pigmentation unaltered. The suprarenal graft was still palpable, the testicle having partially atrophied.

It will be interesting to know the future history of this patient.

C. C. C.

Buzello, A. Ueber die Behandlung der pyogenen Blutinfektion durch intravenöse Anwendung von Urotropin. [**Treatment of pyogenic blood infections with intravenous injections of urotropine.**] *Deutsche Ztschr. f. Chir.*, 1922, **168**, 61.

Buzello recommends the intravenous injection of 40 per cent. solution of urotropine in physiological salt solution for the treatment of pyogenic infections of the blood. Doses of 10–15 c.cm. may be given daily; often great improvement occurs after 2 or 3 injections. If strangury, haematuria, or scalding urine appear, the treatment must be stopped; these symptoms are said to be due not to definite injury of the kidneys, but to the appearance of formalin in the urine; they may appear after 6–8 doses. Otherwise the injections were harmless. 18 cases of pyogenic blood infection were treated, with two fatalities and 16 cures. C. C. C.

Levine, E. C., and **Segall, H. N. Post-transfusion reactions.** *Surg. Gynec. & Obst.*, 1922, **35**, 313–19.

Levine and Segall draw attention to a series of cases in which the blood of patients and donor, compatible before anaesthesia and again 24 hours after the end of operation, were found to be incompatible immediately after prolonged administration of ether. They conclude that the compatibility of donor's and recipient's bloods must be examined before every transfusion. They believe that no transfusion should be done within 24 hours of long ether anaesthesia, even if compatibility was found before operation. They suggest several hypotheses to explain the phenomenon, but reserve their opinion until they have examined these theories more thoroughly.
C. C. C.

Langenskiöld, F. The result of the conservative treatment of tuberculous spondylitis. *Acta Chir. Scand.*, 1922, **55**, 51.

Of 237 cases of Pott's disease treated in hospital, 148 were subsequently traced. The total mortality was 40·5 per cent., and the mortality traceable to the disease of the spine was 37 per cent. Only 22, or 16 per cent., were definitely cured, but in 31 per cent. the result of treatment was good. The incidence of the disease in the cervical, dorsal, and lumbar regions was 16·5, 56·5, and 27 per cent. respectively. The prognosis was best for the cervical region (mortality 24 per cent., good results 70 per cent.) and worst for the dorsal region (mortality 44 per cent., good results 18 per cent.). The disease in the lumbar region showed a mortality of 28 per cent., and good results in 36 per cent. The duration of the disease was from 2 to 20 years, with an average of 7 years. The average residence in hospital of the cases with a good result was 7 months, while it was only 4 months among the cases with a bad result. Home treatment was continued for more than a year in about half the number of cases. Langenskiöld concludes that, though the results depend as much on the nature of the case as on the treatment, a longer stay in hospital, with careful control of home treatment, should yield better results. When this course is not feasible for financial reasons, Albee's bone-grafting operation should be undertaken. R. Hertz (*ibid.*) has treated 305 children with Pott's disease which in 104 cases was complicated by fistulae or abscesses. Five years after discharge 151 patients were traced, of whom 70 per cent. were cured and 25 per cent. were dead.
C. L.

Nielsen, T. Om Ganginvaliditet og Contractura genuum ved Polyarthr. chron. deformans. [B.] [**Disorders of gait and contractions of the knees in chronic polyarthritis deformans.**] *Ugesk. f. Læger.*, 1922, **84**, 693–707.

The impression gained by Nielsen by a study of 109 cases of chronic polyarthritis is that the disorders of gait associated with this disease are almost invariably due, in the first place, to disease of the knee. Among 41 cases of contractions at the knee-joint there were only 3 in which coincident hip disease appeared to be the primary lesion. In 6 other cases there were, indeed, contractions at the hip, but they were secondary to contractions at the knee. Thus, in the overwhelming majority of cases, the restoration of normal or efficient gait concerns the knee. With regard to treatment, Nielsen inveighs against the practice, indulged in even at large hospitals, of encouraging flexion of the knee at rest, with pads and pillows secured in the popliteal space. It is most important to encourage the maintenance of complete extension at rest. Passing on to cases first seen in an advanced stage, Nielsen discusses two methods, both of which he has found useful. The first is resection, which he has practised in 3 cases with excellent results. The indications for this procedure are: unilateral and severe contraction at the knee associated with such advanced destruction of the parts concerned that there is little prospect of success with less drastic treatment. A further indication is a normal condition of the hips.

The other alternative is 'redressement forcé', the dangers of which (exacerbation of the disease, fracture of bone, and rupture of other structures) have been greatly exaggerated. It is true that ankylosis may follow, but it should not, if after-treatment is skilled and prolonged. The forced correction should be made under general anaesthesia, without which the lively pain provoked is apt to prevent both correction and subsequent immobilization in a position of complete extension. This procedure should be adopted when conservative treatment has failed, and should be followed by 2 to 4 weeks' immobilization in plaster. To minimize the risk of paralyses of the muscles, over-extension of the limb should be avoided, but, on the other hand, the risk of relapse to a fixed position of flexion should be countered by securing the limb in the position of normal extension. After-treatment should last for weeks or months, and should consist of massage, active movements, electrical treatment, packs, and baths. Nielsen has achieved marked success in 6 cases treated on these principles, but he also records a disaster, forced correction being quickly followed by gangrene, extending up to a point just above the ankle, and necessitating amputation at the knee. None of the large arteries had been torn, and the gangrene must have been provoked by spasm of the arteries or compression of their walls by adjacent structures. C. L.

Mellon, R. R., Slagle, E. A., and **Acree, S. F. The practical application of 'buffers'.** *J. Am. M. Ass.*, 1922, **78**, 1026–9.

Mellon, Slagle, and Acree record the following interesting case and deal with its practical applications. A certain patient was given a citrate transfusion and had a very severe reaction. The citrate was examined and it was found that the hydrogen-ion concentration was 10·5. The hydrogen-ion concentration of the salt used should have been 8·0. It was obvious, therefore, that the specimen contained free alkali. This was neutralized with acid and the patient had a second transfusion from the same donor without any untoward result. At the same time a student underwent a retransfusion of her own blood which had been drawn into the un-neutralized citrate. She had a similar reaction, but not so severe as that manifested by the patient. The authors describe in detail what is meant by buffering solutions for intravenous use (as was done in this case) and point out the possibility of further practical applications. G. W.

Di Pace, I. Osservazioni su alcune rachianestesie ripetute negli stessi individui. [**Observations on certain cases of spinal anaesthesia repeated in the same individual.**] *Policlin.*, 1922, **30**, Sez. Chir., 311.

Di Pace, speaking from a very considerable experience of spinal anaesthesia, and examining a series of cases of failure, some total, some partial, some with paradoxical manifestations such as hyperaesthesia or convulsive tremor—and especially those cases in which the unusual results were observed in each successive attempt at lumbar injection—comes to the conclusion that technical, pharmacological, and personal errors can be excluded, and that idiosyncrasy must be held responsible. If, he says, quinine, chloral, arsenobenzol, and even chloroform can and do produce, in certain individuals, effects precisely the opposite of those occurring in the vast majority of subjects, it is no more remarkable in the case of novocaine and stovaine, and he believes that in his own cases he can eliminate all other explanations. E. R. C.

Wideröe, S., og **Dahlström, S.** Om lumbalanaestesiens farer. [**The dangers of lumbar anaesthesia.**] *Norsk Mag. f. Lægevidensk.*, 1922, **83**, 450.

In 1921, Guibal published in *La Presse médicale* three cases of paralysis of the respiration following intralumbar injection of stovaine or novocaine. In every case artificial respiration saved the patient's life. This and other publications have drawn from Wideröe and Dahlström an account of investigations made with a view to determining the connexions between the cavities of the skull and vertebral column. Brain (intraventricular) and intralumbar injections were systematically made in five cases of insanity of syphilitic origin, and marked differences were observed in the reactions of the fluids obtained from the two sources. The differences being great, whether they concerned the Wassermann reaction, the number of cells, or the albumin content, it seemed there must be a very faulty communication between the brain and the spinal cord. But intracranial injections of air showed free communication between the lateral ventricles, and intralumbar injections of air showed that this could readily escape to the surface of the brain and into its ventricles, as indicated by the X-rays. Almost immediately after the intraventricular injection of phenolsulphophthalein, it was demonstrable by lumbar puncture, and the intralumbar injection of this dye was followed within five minutes by staining of the fluid in the ventricles of the brain. It is thus evident that stovaine or novocaine injected into the spinal canal can reach the fourth ventricle, and it is, therefore, possible, even probable, that the respiratory paralysis of lumbar anaesthesia is due to the action of the injected anaesthetic on the respiratory centre. C. L.

NEUROLOGY

Wagner von Jauregg. The treatment of general paresis by inoculation of malaria. *J. Nerv. & Ment. Dis.*, 1922, **55**, 369.

Scattered throughout the literature on general paresis of the past hundred years are to found cases in which cure is said to have followed protracted suppuration or fever. As long ago as 1877, Meyer deliberately produced suppuration for this purpose. In recent times, neither mercury nor the arsenical compounds have been able to claim any striking results in the treatment of this disease. The discovery that psychoses were occasionally cured after intercurrent infections led Wagner von Jauregg in 1887 to found a method of treatment based upon this observation. The first attempt consisted in the use of tuberculin injections to produce pyrexia, and it was found that a series of cases so treated lived longer than a control series.

He claims that in this way complete remissions, allowing of the patient's return to work, were frequently obtained. Of a series of cases reported as long ago as 1909, several are still in full possession of their faculties. In the majority of instances, however, return of the symptoms followed. Subsequently, he began to employ hypodermic injections of 'Besredka's typhus vaccine' for the same purpose. Nevertheless, it was found that more striking improvements occurred in patients who had fortuitously developed infections such as pneumonia, erysipelas, or suppurating foci. In 1917, therefore, Wagner von Jauregg began to inoculate cases with benign tertian malaria. Of the first nine so treated, three are even now actively and effectively at work. Since 1919, the method has been used as a routine. The malarial subject from whom the strain in use was originally obtained had acquired malaria in Vienna and had not been treated with quinine. With this strain over 200 cases have since been inoculated. From one to four c.cm. of blood are taken from a previously inoculated general paralytic between two attacks, and immediately injected subcutaneously into the patient to be treated. Typical attacks of benign tertian malaria appear after an incubation period varying from six to thirty-six days. The patient is allowed to have from nine to twelve of these untreated, and then quinine is administered. It is found that the attacks, though typical in character, soon become quotidian, and are much more sensitive to quinine than malaria directly acquired from anopheles. The routine adoption of this method pre-supposes that there is always available a patient already inoculated from a still earlier subject in the series, or alternatively that there is malaria in the district in which it is proposed to use it. In the latter case, blood should be obtained from a subject who has not been treated with quinine. It is claimed that by this method far better results have been obtained than by any other. In early cases a complete remission can be confidently expected. In a series of selected cases, complete, and so far permanent, remissions occurred in over 50 per cent. Improvement sets in gradually after the malarial attacks have ceased. The physical condition responds markedly, epileptiform attacks and speech disturbances cease, and the patient is able to resume his normal life. The Wassermann reaction in blood and cerebrospinal fluid are not modified in these circumstances. For obvious reasons the treatment is most readily carried out in an institution where it is adopted as a routine measure. F. M. R. W.

Craig, C. B., and **Chaney, L. B. Spinal drainage following intravenous arsphenamine.** [**B.**] *J. Nerv. & Ment. Dis.*, 1922, **56**, 97.

In a preliminary review, the authors remark that the impermeability of the choroid plexuses to chemicals in solution in the blood has been a physiological obstacle to the efficacious treatment of syphilis of the nervous system by intravenous medication. Further, such small quantities of arsenic as do reach the cerebrospinal fluid are rapidly removed in the active circulation of the fluid and returned through the arachnoid villi into the blood-stream. Injection into the lumbar theca is not more rational, for it is probable that a purely local application of the drug results. At least Weston's observations point to this conclusion. Recently, various observers have found that better results followed simple drainage of the theca than were obtainable by the different methods of intrathecal medication, and have proposed that intravenous arsenical treatment should be followed by spinal drainage as a routine. The basis of the suggestion is the belief that drainage lowers the cerebrospinal fluid tension and leads to increased secretion of fluid by the choroid plexuses from blood containing the arsenical drug. In these circumstances it seems probable that more arsenic may reach the sub-arachnoid space than would otherwise be the case. The method adopted by the authors is to perform lumbar puncture immediately after intravenous injection of arsphenamine. The patient lies on his side and the cerebrospinal fluid is allowed to run out freely until it begins to drip slowly at the rate of five or six drops a minute. From 15 to 80 c.cm. may be withdrawn in this way. The results obtained in thirteen cases of tabes, tabo-paresis, and general paralysis are recorded in detail.

As many as twelve weekly drainages are carried out in a single case. As far as can be judged from the authors' tables, the cerebrospinal fluid Wassermann reaction and globulin content are relatively unaffected by treatment, but the cell-content of the fluid diminishes appreciably. They conclude that no single method of treatment is universally applicable. The method of choice is intravenous arsphenamine, followed by repeated spinal drainage, which is not a hazardous procedure. Some cases which have ceased to improve under simple intravenous treatment may be further benefited by these means. The serological results are as good as those obtained after intrathecal treatment, and the severe root pains which often follow the latter do not occur. F. M. R. W.

Bielschowsky, M. Weitere Bemerkungen zur normalen und pathologischen Histologie des striären Systems. [B.] [**Further observations on the normal and pathological histology of the striate system.**] *J. f. Psychol. u. Neurol.*, 1922, **27**, 233.

I. Chronic chorea. Bielschowsky reviews earlier work on the morbid histology of this condition, citing Jelgersma as the first to localize the essential lesion in the striate system (1908). The later work of Alzheimer, Pierre Marie, and Lhermitte, and of Margulies and others has given precision to and confirmed Jelgersma's observations. Marie and Lhermitte regard the primary disease process as inflammatory, as a chronic encephalitis of unknown toxic origin. Margulies, on the other hand, suggested a congenital and progressive gliosis, to which the parenchymatous lesions are secondary. Most observers agree with Alzheimer that a degenerative process in the nerve-cells of the cerebral cortex, corpus striatum, and subthalamic nuclei is in question. In any case, there is no longer any doubt that the basis of the chorea is a lesion in the corpus striatum. Bielschowsky has carried out a detailed histological examination of four cases of chronic chorea. Two of these have been reported by C. and O. Vogt, who examined the brains by the Weigert method (cf. *Medical Science*, 1922, **6**, 287). Bielschowsky is concerned with the finer cellular histology. He finds that the essential lesion is nerve-cell 'necrobiosis' in the caudate nucleus and putamen. The small cells die earlier than the larger cells, but there is no question of a selective small cell lesion. The lesions in the globus pallidus and subthalamic nuclei are secondary.

II. Progressive rigidity. (Cf. C. and O. Vogt, *Medical Science*, 1922, **6**, 287.) In this condition, tremor of the paralysis agitans variety is gradually replaced by diffuse muscular rigidity. Bielschowsky reports a single case. The lesion is the status fibrosus of the Vogts, in which the striatum is involved at first and the pallidum later. He finds that the essential lesion is a degeneration of nerve-cells and fibres in the striatum (caudate nucleus and putamen). The small nerve-cells had completely disappeared, and only a few of the larger type remained. The pallidum and sub-pallidal nuclei were similarly but much less intensely involved. Secondary nerve-fibre degeneration had resulted. The ground substance was spongy in appearance, there were astrocytes and excess of glia fibres. There were also diffuse cell lesions in the third layer of the cerebral cortex. The later developing disease in the pallidum and sub-pallidal centres is regarded as responsible for the replacement of tremor by rigidity. In this section, Bielschowsky deals in detail with Ramsay Hunt's observations (*Brain*, 1917, **40**, 58) on juvenile paralysis agitans, which this writer has attributed to a selective degeneration of the 'globus pallidus system of cells'. He rejects the histological basis of this work and the views founded upon it.

III. Paralysis agitans. Jelgersma was the first to formulate the modern conception of the pathology in this disease. Bielschowsky agrees that the essential lesion is in the globus pallidus, but adds 'despite the stereotyped character of the clinical picture in this disease, I regard it as most unsuitable material for the basis of any views of localization, because the distribution of the pathological change is too general. It is probable, however, that there is a marked striate component in the clinical picture.' The Vogts named the lesion 'status disintegrationis'. It includes degeneration of nerve-cells and fibres, small foci of haemorrhage, and softening, leading to the formation of lacunae, and a rarefaction of the tissue surrounding the vessels. All these changes are to be regarded as a manifestation of a premature senility of the whole brain, involving the striatum and pallidum predominantly. When tremor dominates the clinical picture, the striatum bears the brunt of the disease, and when rigidity is prominent the pallidum. He rejects Tretiakoff's view that the essential lesion is in the substantia nigra. He has examined six brains. He finds marked vascular lesions, capillary fibrosis, and 'angio-sclerosis' of the larger arteries and veins. All the layers of the vessel walls are atrophic, and the media shows hyaline degeneration. In section, small transparent areas are seen round the vessels. They are the basis of the lacunae which appear at a later stage. The normally homogeneous ground-substance becomes spongy and reticular in structure. In the striatum both types of ganglion cell are involved, showing Nissl's chronic cell process with lipoid degeneration. A similar condition is found in the pallidum, and both contain abundant degeneration products of lipoid nature. Secondary fibre degeneration results from the cell lesions, involving strio-pallidal fibres, pallidal fibres, the ansa lenticularis, and Forel's H fields. Bielschowsky regards the vascular lesion as primary, the parenchymatous and ground-substance changes as secondary.

IV. Pseudo-sclerosis and progressive lenticular degeneration. The work of Wilson, Alzheimer, Spielmeyer, and others is reviewed. He concludes that these diseases are members of a group with a variable somatic and psychical symptomatology. As to the pathological basis, Spielmeyer believes that there is no essential difference between the two, but that they are variations of the same disease process. Nothing is known of the aetiology. Bielschowsky examined a single example histologically. It does not appear to have been a characteristic case clinically, for it had a twenty years' course. There were symmetrical lesions in the putamina, confined to the dorso-lateral parts of these structures and scarcely affecting the pallida. The lesion consisted of a spongy degeneration of the ground-substance, regressive changes in the nerve-cells and fibres, and the presence of abundance of degeneration products in the affected areas. These changes are described in great detail.

Bielschowsky correlates his observations with the Weigert examinations of the Vogts, and the paper should be read in association with their work. The lesions are described in minute detail, and are illustrated by a small series of plates. F. M. R. W.

Cushing, H. Further concerning the acoustic neuromas. *Laryngoscope*, 1921, **31**, 211.

Cushing believes that early and precise diagnosis and localization is more constantly and certainly attainable in the case of acoustic neuromas than is the case with intracranial tumours elsewhere. Since the publication of his monograph on this subject, in 1918, forty-seven additional cases of the kind have come under observation and treatment. As before, they represent 7·3 per cent. of all verified intracranial tumours, 24·5 per cent. of all infratentorial tumours, 60·3 per cent. of all extra-cerebellar tumours, and by far the greater percentage of all tumours with symptoms referable to the cerebello-pontile angle. He concludes that when tumour symptoms point to the angle as the seat of the lesion and begin with deafness we may be fairly certain that we are dealing with an acoustic neuroma. He gives clinical reports of several cases in which, despite the now readily recognizable picture of acoustic neuroma, errors of diagnosis were made, in some instances avoidable errors. In all these instances prolonged aural and nasal local treatment had been employed and the signs of intracranial tumour unnoticed or misinterpreted. In this connexion it may be mentioned that the paper was originally read before an otological and laryngological society. There are also described a case of endothelioma of the Gasserian envelopes, which gave a picture of acoustic neuroma, and one of glioma (?) originating in the eighth nerve nucleus and giving a similar clinical picture. Discussing the method of surgical approach to acoustic neuromata, he expresses the view that partial enucleation is all that can be attempted, until precise diagnosis allows of intervention at a much earlier stage than is now commonly possible. In conclusion, he states his objections to the translabyrinthine operation advocated by Fraser of Edinburgh. F. M. R. W.

Bremer, F. Global aphasia and bilateral apraxia due to an endothelioma compressing the gyrus supramarginalis. *Arch. Neurol. & Psychiat.*, 1921, **5**, 663.

Bremer reports the case as one in which, owing to the small size and well-defined character of the tumour, reliable information as to cerebral localization was obtainable. The patient was a man of 60 who, during the year 1920, had five epileptiform attacks associated with numbness and clonic movements in the right arm and loss of speech. He came under observation while in an attack. He could not understand spoken speech, and his speech was limited to saying 'I don't know'. Examination further revealed paresis and astereognosis of the right arm and 'global aphasia'. There was also ideo-motor apraxia. He was quite unable to handle familiar objects placed in his hand appropriately. He was fully conscious and co-operated well in his examination. The left optic disk showed slight blurring of the temporal margin. A diagnosis of left post-central tumour was made, and at operation Cushing enucleated an endothelioma of 4 by 3·5 cms. from the surface of the supramarginal gyrus. Following operation there was slight paresis of the right arm, but no other signs of hemiplegia. Apraxia persisted in both arms. Speech recovered partially, showing some dysarthria and perseveration. After three months recovery of all symptoms was practically complete. Some excellent photographs accompany the case record.

Bremer concludes that the case agrees with the notion generally held that bilateral ideo-motor apraxia may be produced by a lesion of the left supramarginal gyrus. The almost complete absence of general intracranial tension symptoms allow us to assume that pressure on the corpus callosum was not in question. F. M. R. W.

de Kleijn, A., u. Magnus, R. Labyrinthreflexe auf Progressivbewegungen. [**Labyrinthine reflexes elicited by movement.**] *Arch. f. d. ges. Physiol.*, 1921, **186**, 39.

In a recent number of *Medical Science* (1922, **7**, 109) the work of Magnus and de Kleijn on the nervous regulation of posture was briefly summarized. These observers have found that in so far as the component reactions in this regulation are labyrinthine in origin they arise in the otolith organs and are not a function of the semicircular canals. In the present paper they are concerned with labyrinthine reflexes elicited by movement of the animal through space. Guinea-pigs, rabbits, cats, and dogs were employed in the experiments, and all gave similar results.

Among the reactions described is the 'Liftreaktion'. The animal is placed sitting on a horizontal board, which is then rapidly raised or lowered vertically. When it is raised, at the moment when movement begins the animal sinks down on its flexed forelimbs, and the head declines also. At the moment of cessation of movement, the forelimbs extend and the head and the fore part of the trunk are raised. These movements are reversed when the board is lowered. They are all abolished by bilateral ablation of the labyrinths. If the animal be held vertically in the hand and the head tilted so that the snout points vertically, it is found that horizontal movements on a dorso-ventral axis also elicit the same reactions; movement ventral-wards corresponding to lowering of the horizontal board and movement dorsal-wards to raising it. In this way it has been determined that the essential stimulus for the reaction is movement of the head through space along its dorso-ventral axis.

Other reactions, which ensure that the animal jumping or falling from a height shall alight upon its spread toes and extended forelimbs, are also described. It is found that, like the 'Liftreaktion', these are abolished by ablation of the labyrinths. On the other hand, such various procedures as de-afferentation of the muscles taking part, removal of the forebrain and the greater part of the cerebellum, or putting the otoliths out of action by centrifugalizing the animal (guinea-pig) do not interfere with their activity. From all these observations, the authors conclude that the labyrinthine reflexes on movement arise exclusively in the semicircular canals, are produced by movement through space and not by variations in posture, and have their reflex centres entirely within the brain-stem. They may be contrasted with the static or postural reactions, which are produced by variations in the position in space of the maculae and otoliths. Both groups appear to have their central nervous representation in the brain-stem. In this way a differentiation of function within the membranous labyrinth has been established, and it has been determined that a complete representation exists in the brain-stem motor centres for all the movements and postural reactions of the animal. F. M. R. W.

Kihn, B. Über die sogenannte Beri-beri der Affen und der Tiere überhaupt. **[On the so-called beri-beri of monkeys and of animals in general.]** *J. f. Psychol. u. Neurol.*, 1922, **27**, 316.

Kihn discusses the protean clinical and pathological manifestations of beri-beri, and also the question of the identity of the human with the experimentally produced forms of the disease. In a short comparative clinical study of the two, he adopts Mense's classification of human beri-beri into 'acute pernicious', 'wet', 'dry spastic-atrophic', and 'mild' forms, and proceeds to contrast these with the symptomatology as seen in different animal species. In *pigeons* an ataxic gait, muscular weakness, and slight sensory changes are the early symptoms. Later, abnormal attitudes and involuntary movements develop, followed by epileptiform convulsions and death. He also refers to an asphyxial form. In *fowls* a similar clinical picture may be seen, though there is said to be a greater tendency to peripheral nerve symptoms and to paralyses of flaccid type. In the case of pigeons he speaks of 'spastic' paralysis. In *rats* involuntary movements and attitudes are prominent, and are referred to cerebellar and labyrinthine lesions. In *monkeys* the disease approximates more closely to the human type, though here also, according to Schaumann, symptoms like those seen in rats may be prominent. Significantly enough, *guinea-pigs* do not react to an appropriate diet by developing beri-beri, but instead show signs of scurvy, a strange fact, which has as yet found no explanation. He gives a similar comparative review of the nervous lesions in the different human and experimental forms of the disease, but he does not mention that in the acute pernicious forms, and in infantile beri-beri, no unequivocal lesions in the nervous system may be found. Parenchymatous peripheral neuritis was the earliest lesion to be described in man and animals, but more recent investigations have revealed the frequent but inconstant presence of nerve-cell changes in brain and cord, and of degenerative lesions in central nerve-fibre systems. In rats, also, punctate haemorrhages in brain-stem and cerebellum have been described.

These extremely variable clinical and pathological findings lead Kihn to express the doubt that we may be dealing with more than a single pathogenic agent, and that the human and experimental forms may not be identical. It is clear that he, like other students of the problem, is perturbed by the conflict of opinion, not alone as to the facts of clinical and pathological observation, but also as to the conclusions to be drawn from them. He believes that the wide range of animal species under examination may account for some of the differences, the presence of adventitious factors for others, but that there remains much obscurity which in the present state of knowledge cannot be resolved.

We think that there can be little doubt that the information at our disposal does not yet allow of a final determination of the causes operative in the production of beri-beri, but that much of the conflict of opinion and of the confusion of thought and expression to be found in the vast literature on the subject is even now capable of resolution—of a resolution which is an essential preliminary to further progress.

In the attempt to assess the value of the clinical and pathological facts of observation, in respect of both human and experimental forms of the disease, we shall meet with almost unsurmountable difficulties unless we are so fortunate as to possess some first-hand acquaintance with both, for the accounts to be found in the literature are not sufficiently complete or consistent to form the basis of any reasoned conclusions. It is, perhaps, inevitable that this should be so, for familiarity with the technique of exact neurological investigation, and with the modes of reaction of the nervous system to disease, can but rarely form part of the equipment of either experimental worker or student of tropical diseases, from whom most of our information is derived. Indeed, it requires but a short acquaintance with the literature to bring this forcibly home to the reader, for it abounds in artificial clinical classifications, in misuse of neurological terms, and in fallacious interpretations of symptoms and of lesions, all arising from the fact that the writers have not an adequate general knowledge of neuropathology by which to orient themselves and to obtain a sense of proportion. Mense's classification is of this conventional and misleading character, and its continued adoption excludes a scientific conception of the disease. Hamilton Wright, whose clinical studies of human beri-beri are, as far as we have found, quite unequalled, has defined the acute pernicious type, which stands by itself as predominantly or even entirely cardiac in symptomatology and pathology. However, in respect of the other three types, we believe that no fundamental distinction can be drawn between them. If we take acute pernicious beri-beri as standing at one end of the series of clinical types, we find at the other cases of polyneuritis of moderate severity associated with signs of myocardial degeneration, which may give rise to no more than an 'effort syndrome' of mild grade, such as may be found in toxic polyneuritis from any cause. Intermediate between these extremes we find a series of cases in which the symptoms may be divided into three groups, nervous, cardiac, and a group including oedema and serous effusions as its components.

The two first groups are constantly present in a roughly direct proportion in respect of intensity. Thus we have cases of severe rapidly developing polyneuritis leading to profound muscular weakness with ultimate wasting, contracture, and deformity. In other cases, the polyneuritis is less severe in degree and less acute in onset, and may not be associated with severe wasting or contracture in the affected muscles. Similarly, we meet with varying grades of myocardial involvement. In a certain number of instances we have superadded to these symptoms oedema and serous effusions. These also vary in severity from cases of profound general anasarca to others in which there is slight oedema round the ankles. There seems to be no direct relationship between this group of symptoms and those included in the two first groups, so that we may meet cases in which oedema of extreme severity may co-exist with polyneuritis and cardiac involvement of relatively slight intensity. This, indeed, seems to be the basis of the attempt to divide 'ship beri-beri' from the forms arising on land. In spite of the contrary opinion, study of the records of ship beri-beri indicate that polyneuritis is constantly present, but may be masked to superficial observation by the presence of oedema and of scorbutic manifestations. We see, therefore, that the only difference between wet and dry beri-beri is in the presence in the former of an additional symptom, oedema and serous effusion. There is no other fundamental distinction. In the misuse of the term 'spastic' in connexion with the fibrous degeneration of paralysed muscles in so-called dry beri-beri, we see another source of confusion. The word is also applied, and with equal inaccuracy, to the convulsive muscular spasms sometimes seen in rice-fed pigeons. We have never found it to be employed in its true sense. The point may appear trivial until we realize that its misuse leads the unwary reader to suppose that he is dealing with paralysis of central origin, that is, with the spastic paralysis of the neurologist. From this it is but a short step to the prevalent conclusion that the symptoms of beri-beri are the result of the chromatolytic changes sometimes found in nerve-cells of the cerebral hemispheres in human and avian beri-beri. Similar inexactitudes are to be found in the use of the expression 'cerebellar fits'. As far as we can gather from the literature and from a limited observation of rice-fed pigeons and fowls, these attacks are either symptoms of vestibular disorder, rolling movements, and abnormal attitudes and gait, or of asphyxia, or both combined, and it is by no means clear why they should have been identified with cerebellar fits. When we turn to the morbid anatomy of the nervous system in beri-beri we meet with similar errors, and with some of these we have dealt in previous numbers of *Medical Science* (1920, **2**, 41, and 1922, **5**, 314). It would be both tedious and superfluous to continue this examination of the literature. We have seen enough to realize that much of the conflict and confusion existing arises in all probability from avoidable causes and is not inherent in the problem. We believe that the whole matter might be materially simplified were it approached from a broad neuropathological standpoint. We have only to compare the clinical and pathological features of the disease with those found in other diseases of the nervous system, to take into account what might be called the time and intensity factors, and to appreciate the differences in structure and metabolic activity between animals so far removed as pigeons and man, to appreciate that an extreme degree of variability in the manifestations of the disease is to be anticipated, and we are not compelled to imagine that we are dealing with numerous and separable conditions. If we take the relatively simple case of alcoholic poisoning in man, we can readily see this. The individual poisoned by alcohol may suffer from delirium tremens or from chronic polyneuritis with Korsakow's psychosis, according to the time and intensity of the factors operative. It occasions no surprise that the nervous lesions in the two instances differ widely, and because the brain of the patient dead of delirium tremens shows widespread chromatolytic changes in the cortical nerve-cells, we do not find pathologists arguing that the paralysis of polyneuritis from chronic alcoholism is due to cortical nerve-cell degeneration, and that the parenchymatous peripheral neuritis 'has nothing to do with the case'. Yet the literature on beri-beri abounds in such otiose discussions. When we come to compare the beri-beri of pigeons with that of man, the disparity in circumstances is even wider than those we have mentioned in the case of alcohol, while, in addition, the assessing of symptoms is infinitely more difficult in small animals. The present reviewer has on several occasions had the opportunity of examining monkeys suffering from paralyses of obscure nature, and he has been immensely struck by the difficulty both of eliciting physical signs in any but the most casual fashion and of interpreting those found. In the circumstances, therefore, it seems impossible to form any conclusions of value from the combination of incomplete observation and premature conclusion that so commonly passes for clinical record in the literature on beri-beri. This disease presents problems to workers in almost every branch of biological science, not the least important of which centres in the reaction of the nervous system to vitamin B deprivation and to the metabolic disorders arising therefrom. It can only be adequately studied in relation to other known forms of reaction of the nervous system to pathogenic agents, more especially in relation to the effects of such poisons as alcohol, arsenic, and the toxin of diphtheria, to mention the most important. So strikingly does beri-beri, in respect both of its cardiac and its nervous manifestations, resemble the intoxications produced by these poisons that we cannot refrain from the speculation that there must be a fundamental factor common to them all. We have urged in earlier numbers of *Medical Science* that beri-beri may be an intoxication of endogenous origin, but clearly the question cannot be left there. We have to determine how alcohol acts as a poison and interferes with the structure and functions of nervous tissue, and when we have found the answer to this question we shall be much nearer to a comprehension of the pathogenesis of beri-beri. F. M. R. W.

TINEL, J., et **SANTENOISE, D.** Vago-sympathique et anaphylaxie. [**Vagotonia and anaphylaxis.**] *Presse méd.*, 1922, **30**, 321–3.

Tinel and Santenoise discuss the application to the study of epilepsy of recently acquired knowledge concerning haemoclasis. The first part of their thesis is that paroxysms are characterized by the now well-known features of leucopenia, &c. They have been able to foretell the occurrence of paroxysms by blood examination, but admit that there are many difficulties in elucidating the whole picture in any one case. They cite four cases in detail. Their second point is that periods of liability to paroxysms are characterized by a general lowering of the threshold for anaphylactic phenomena, so that digestive haemoclasis can usually be demonstrated at these times. This state of generally heightened susceptibility they next associate with other signs of vagotonus, emphasizing in particular the oculocardiac reflex. Finally they assert that the condition to which the name vagotonia is given is the groundwork of epilepsy. Those drugs which control epilepsy are those which calm the instability of the vagotonic. They further develop the interesting consideration that the taking of food is contra-vagotonic; it produces a haemoclasic crisis and, as it were, discharges the batteries for the time. They consider that this explains the common occurrence of epilepsy at night and particularly towards morning. The patient having then been without food for some time, the vagotonic irritability has been built up again and the inevitable explosion takes place.

G. W.

Parsons, A., MacNalty, A. S., and Perdrau, J. R. Report on encephalitis lethargica. *Reports on Public Health and Medical Subjects, No. 11, Ministry of Health,* 1922, pp. 344, price 10*s*.

The scope of the report is indicated by its sub-title, 'an account of further inquiries into the epidemiology and clinical features of the disease; including an analysis of over 1,250 reports of cases notified in England and Wales during 1919 and 1920, together with a comprehensive bibliography.' In addition, there is a preface written by Sir George Newman, and sections on the pathology and bacteriology of encephalitis. Thus the report contains a wealth of information on every aspect of the disease, and will become a valuable work of reference on the subject.

Within the scope of a short notice but a few of the salient features can be referred to, and we will not attempt any appreciation of the pathological sections here, but will leave them for discussion elsewhere. In the epidemiological section, Dr. Parsons concludes that there is no justification for the view that influenza and encephalitis lethargica are in any way related, or that an attack of the former disease predisposes the individual to the latter. Further, there is no convincing evidence connecting the so-called 'epidemic hiccough' with encephalitis. In the matter of age incidence, although no age is found to be exempt, the second decade of life seems to provide the majority of cases. Fifty cases occurring in pregnant or lying-in women are reported. In these circumstances every clinical type of the disease has been observed, but stress is laid upon the frequency of profound psychical disorders and of somatic symptoms of an active character, such as acute choreiform manifestations. There seems to be no special liability to miscarriage under these conditions. Three cases of encephalitis neonatorum ending in recovery and two fatal cases have been reported, the result of the disease in the pregnant mother.

In the clinical section, Dr. Parsons has utilized MacNalty's clinical grouping into types as follows: I. *Cases with general nervous disturbance but with no focal symptoms.* II. *Cases with both general and focal symptoms.* These are subdivided into: (*a*) cases with third nerve palsies; (*b*) cases with brain-stem and bulbar symptoms; (*c*) cases with symptoms referable to an affection of the long tracts; (*d*) cases with cerebellar symptoms; (*e*) cases with symptoms referable to the cerebral cortex; (*f*) cases with spinal cord symptoms; and (*g*) cases with peripheral nerve symptoms. III. *Mild cases.* For the description and placing of individual symptoms, the method of classification first formulated in this journal (1920, **3**, 51) and later amplified in *Brain* (1920, **43**, 197) is used. It is based upon Hughlings Jackson's teaching on 'positive' and 'negative' symptoms, and is complementary to the anatomical scheme of MacNalty.

The mode of onset of the disease is discussed and analysis of the available records indicates that the commonest initial symptoms are, in order of frequency, headache, lethargy, vomiting, diplopia, changes in disposition, fever, diffuse pains and malaise, constipation, and defective vision. While a subacute onset is the rule, acute and even sudden onset has been recorded. The symptoms of the fully-developed disease are analysed in detail, and there are short sections on relapses, complications, sequelae, treatment, and prophylaxis.

Over 1,250 case records have been analysed in the making of the present report, but quotations and some of the statistical tables make it clear that the information has been of very unequal value. Accounts have been received from the provinces of so-called mild forms of encephalitis, in which there is no apparent justification for the diagnosis, unless our conception of the disease is to be so wide as to become wholly indefinite. This type of difficulty is inherent in the compilation of reports based upon information from sources of unknown value, and while the experienced clinician will readily detect the sources of fallacy arising in this way, the reader unfamiliar with encephalitis lethargica is likely to gain a somewhat loose and erroneous notion as to what it is reasonable to regard as a case of the disease.

In the matter of clinical classification it is probable that the two complementary schemes adopted in the report provide as useful a working method as is at present available. It is now recognized, in this country, if not in France, that a purely clinical basis of classification is useless and leads to infinite confusion, owing to the kaleidoscopic course which any given case of the disease may run; nevertheless, MacNalty's anatomical scheme is capable of considerable improvement. Thus, reference to his groups under Type II shows that there is no place for that large group of cases presenting a clinical picture akin to that of paralysis agitans, in which the basal ganglia and subthalamic nuclei appear to bear the brunt of the disease process. Further, we do not believe that his group (*c*) has any independent existence. All the cases under this heading must belong primarily to one or other of groups (*b*), (*d*), (*e*), or (*f*). In respect of Type III, which includes so-called 'mild cases', the experience of the past two or three years indicates that we must materially modify our notions as to what we mean by a mild case. MacNalty appears to use the term in an extremely narrow sense, namely, as applied solely to the initial constitutional symptoms. A very large number of patients now presenting some variety of paralysis agitans symptom-complex date their trouble from an apparently trivial illness, which was diagnosed as 'influenza', 'a cold', a 'nervous breakdown', or as 'hysteria'. To regard such cases as mild is absurd, for it is here that encephalitis presents its most crippling effects. Moreover, since weeks or months may elapse between the initial ailment and the development of Parkinsonian symptoms, we can scarcely be justified in regarding a case as mild within a year of its onset. This brings us naturally to the question of residual nervous symptoms in encephalitis. Evidence is now accumulating to the effect that it is extremely rare for patients who survive the acute stage of encephalitis to be restored to normal health. Recovery in any but the surgical sense of the term is the exception. The commonest of all sequels, occurring in over 40 per cent. of cases according to one authority (cf. *Medical Science*, 1922, **6**, 311), is the development of some variation of the paralysis agitans syndrome. On this question of end-results the report is both inadequate and misleading. Paralysis agitans as a sequel is dismissed in a footnote, though its occurrence is now a commonplace of clinical neurology.

Nevertheless, by correlating the information obtained from this and other sources on the after-effects of encephalitis, we gain some interesting information as to the nature of certain of the striking motor symptoms of the disease.

In the classification of clinical forms of encephalitis referred to earlier as having appeared in this journal and elsewhere in 1920, we included under the heading of 'positive symptoms' not only phenomena of 'release' such as tremor, rigidity, and athetosis, but also such ‘irritative’ manifestations as Jacksonian fits, the so-called ‘myoclonic’ twitchings of muscles and of parts of muscles, and also the acute chorea seen in some cases. The notion of ‘irritation’ as a factor in the production of positive symptoms is at present out of favour, partly on account of the abuse of the term during the last century, partly because it is not understood, but more largely on account of the teachings of Jackson. Nevertheless, the clinical study of cases of head injury and certain physiological observations on the oxygen needs of nervous tissue have made it quite clear that the conception of ‘release of function’ does not explain all positive symptoms, and that we have also to take into account the question of abnormal excitability of nervous tissues as an important factor. It was suggested that the acute chorea of encephalitis, Jacksonian fits, and myoclonic contractions were phenomena of this order. Probably no one would dispute this in the case of Jacksonian fits. However, the conspicuous absence of all three symptoms among the residual effects of encephalitis confirms this view of their origin. On the other hand, the manifest release symptoms, tremor, athetosis, and muscular rigidity are common sequels. Recent clinical and pathological work on the corpus striatum has led certain authorities to the conclusion that involuntary movements of the chorea and athetosis varieties arise as release symptoms in the pallidum when a destructive lesion of the striatum (putamen and caudatus) releases this structure from normal control. In a word, the involuntary movements in Sydenham's chorea and Huntington's chorea are both regarded as phenomena of release. There is no difficulty in accepting this view of athetosis and of the movements of Huntington's chorea, but it is impossible to credit that the wild motor unrest of acute Sydenham's chorea in an adult, or of the acute chorea of some cases of encephalitis can have this origin, especially when we take into account the associated mental excitement. To stand by the bedside of such a patient is to be speedily convinced of the hopeless inadequacy of any theory of pallidal or other release as an explanation of what we see. The course of the condition points in the same direction. It would seem reasonable to conclude therefore that the study of such diseases as Sydenham's chorea and encephalitis lethargica, especially of the end-results of the latter, may help to serve as a corrective of the deceptive simplicity of theoretical notions based upon the pathology of certain chronic nervous diseases. We believe that the careful study of acute nervous maladies and injuries is of greater importance in this connexion than is commonly realized. Apart, therefore, from its obvious value as a source of information on a particular disease, the report under review has an interest for those interested in neurology in the widest sense of this term. F. M. R. W.

PATHOLOGY

Dodds, E. C. Variations in the diastatic power of the urine in relation to its reaction, with a suggested method for the estimation of the diastase content. *Brit. J. Exper. Pathol.*, 1922, **3**, 133.

The original technique for the diastase reaction is criticized because it takes no account of the varying reaction of normal urine. It was proved that the optimum reaction for urinary diastase in the presence of phosphate was P_H 6·1, as in the case of the salivary diastase compound. A modified technique is described whereby the urine is diluted with a phosphate buffer solution, thus bringing all urines to the optimum P_H before its starch-digesting power is tested. Ammoniacal decomposition, by making the urine more alkaline, decreases the diastatic power as determined by the old method, but has no effect on the method suggested. Diastase tends to cling to urinary deposits, hence all urines should be well shaken before the estimation is performed. E. C. D.

Gayda, T. (1). Ricerche di calorimetria. Il calorimetro differenziale. [**Investigations on calorimetry. The differential calorimeter.**] *Arch. d. Fisiol.*, 1921, **19**, 1.

Gayda, T. (2). La produzione di calore nello sviluppo ontogenetico del bufo vulgaris. [**Heat production during the development of *Bufo vulgaris*.**] *Ibid.*, 1921, **19**, 211.

Gayda, T. (3). La tonalità termica nella coagulazione del sangue. [**On 'thermic tonality' in blood-clotting.**] *Ibid.*, 1921, **19**, 255.

Gayda, T. (4). La 'tonalità termica' nella coagulazione del latte. [**On 'thermic tonality' in the coagulation of milk.**] *Ibid.*, 1921, **19**, 261.

Gayda, T. (5). La produzione di calore nei girini alimentati con tiroide o con timo. [**The production of heat in tadpoles fed on thyroid or thymus.**] *Ibid.*, 1921, **19**, 267.

Gayda, T. (6). La produzione di calore nella rana in diverse condizioni sperimentali. I, II, III. [**The production of heat in the frog in various experimental conditions. I, II, III.**] *Arch. d. sc. biol.*, 1921, **2**, 318.

Gayda, T. (7). La produzione di calore nella rana spancreata. [**The production of heat in the frog deprived of the pancreas.**] *Gior. d. r. Accad. med. di Torino*, 1922, **84**, 401.

Gayda, T. (8). La produzione di calore nella rana privata delle capsule surrenali. [**The production of heat in the frog deprived of suprarenal glands.**] *Ibid.*, 1922, **84**, 403.

Gayda, T. (9). Contributo allo studio della fisiologia della tiroide nella rana. [**Contribution to the study of the physiology of the thyroid gland in the frog.**] *Ibid.*, 1922, **84**, 405.

Investigations were carried out by means of a slightly modified Hill's differential calorimeter, of which the author gives a detailed account, together with the description of various experiments intended to determine its loss of heat and establish its thermal capacity. In the ova of *Bufo vulgaris*, immediately after fecundation, the production of heat averages 0·037 cal. per hour and gramme. It then rises and reaches about 0·27 cal. when the tadpole leaves the egg. When this begins to swim it reaches a maximum of 0·95 cal. It then gradually decreases to about 0·34 cal. at the end of the metamorphosis. The increased production of heat in the developing eggs appears to be due to the formation of the segmentation sphere while the volume of the whole egg remains practically unaltered. The increased heat production observed in the tadpoles is probably connected with the muscular contractions necessary for swimming. The subsequent decrease appears due to the diminished relation between body surface and volume. The total quantity of heat produced by the developing eggs in 8 days averages 30 cal. per gm. or 0·12 cal. per egg. That produced by the tadpoles in 120 days is approximately of 1·668 cal. per gm. of tadpoles and of 67 cal. per tadpole. The total quantity of heat produced by one gm. of tadpoles while doubling their body-weight is the greater the older are the tadpoles. The heat-production in adult toads is approximately the same as in tadpoles; it oscillates between 0·29 and 0·51 cal. per hour and gm. of body-weight; it is greater in males than in females.

During the change of fibrinogen into fibrin, the retraction of the clot, the transformation of caseinogen into casein, the precipitation of calcium caseinate, and the retraction of the latter, no 'thermic tonality'[1] is produced.

In tadpoles fed on thyroid the production of heat is greater than in those fed on meat. In tadpoles fed on thymus the same fact can be observed, but in a much slighter degree. The greater production of heat in thyroid-fed tadpoles is due to increased energetic exchanges, while the slightly increased heat-production in thymus-fed tadpoles is connected with the greater amount of food which they ingest.

In the fasting frog the production of heat is constant if the temperature and oxygenation of the water in which it is kept are constant. The heat-production is greater in frogs recently captured than in those kept for some days in the laboratory. Individual differences are also great. At 13° C. the heat-production oscillates in males between 0·236 and 0·795 cal., in females between 0·196 and 0·562 cal. per gm. and hour. In the normal frog the heat-production increases as the temperature of the water in which it is kept is raised. But at 37° C. the frog becomes inexcitable and the heat-production diminishes. Otherwise, at 37° C., the heat-production, referred to 1 cm. of body surface, would be 0·558 cal. per hour, viz. about 1/8 of the value obtainable from homothermal animals in the same experimental conditions. There are no differences as regards heat-production between summer and winter frogs. In frogs perfused with Tyrode's fluid isotonic with frogs' blood-serum, the heat-production, the number of red corpuscles, and the quantity of oxygen in the blood are smaller than in normal frogs. These results are not influenced by feeding with meat or substituting glucose for most of the NaCl of the perfusion fluid. An injection of curare or of nicotine causes a diminution in heat-production. This appears due in the case of curare to the disappearance of the muscular tonus, in the case of nicotine to the paralysis of the central nervous system and motor nerve-endings. One injection of atropine causes an increase in the heat-production which is probably connected with a state of cerebral excitation and of diminished trophic action on the part of the vagus. The removal of pancreas has no effect on heat-production in frogs. After partial removal of the adrenals the production of heat decreases to 30 per cent. of the normal. If the remains of the adrenals become necrotic a further diminution is observed on the day preceding the death of the animals. The removal of the thyroid, the feeding on thyroid, and the grafting of small pieces of the same gland have almost no effect on heat-production in adult frogs. C. D. F.

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[1] The author does not give any explanation as to the exact meaning of the term 'thermic tonality'. In the two papers mentioned above he uses it to indicate the amount of heat produced by an inert body when changing physical status.—C. D. F.

BACTERIOLOGY

Kendall, A. I. (1). **The significance and quantitative measurement of the nitrogenous metabolism of bacteria.** *J. Infect. Dis.*, 1922, **30**, 211.

Kendall, A. I., and **Haner, Reba, C.** (2). **The nitrogenous metabolism of *B. dysenteriae* (Shiga), *B. typhosus*, *B. paratyphosus alpha*, and *B. paratyphosus beta*.** *J. Infect. Dis.*, 1922, **30**, 225.

Kendall, A. I., and **Bly, R. S.** (3). **The nitrogenous metabolism of *Bacillus coli*.** *J. Infect. Dis.*, 1922, **30**, 239.

Kendall, A. I., **Haner, Reba C.**, and **Bly, R. S.** (4). **The nitrogenous metabolism of the Schmitz bacillus.** *J. Infect. Dis.*, 1922, **30**, 245.

Kendal, A. I., and **Day, A. A.** (5). **The nitrogenous metabolism of *Bacillus alkalescens*.** *J. Infect. Dis.*, 1922, **30**, 248.

Kendal, A. I., **Cheetham, H. C.**, and **Hamilton, C. S.** (6). **The nitrogenous metabolism of *Bacillus proteus*.** *J. Infect. Dis.*, 1922, **30**, 251.

In the first of these papers the author investigates the amounts of the various nitrogen fractions produced in different media by bacteria. The nitrogen fractions are divided into 'protein nitrogen' and 'non-protein nitrogen'. The sum of these is the 'total nitrogen'. The non-protein nitrogen is again divided into 'amino-nitrogen', 'ammonia-nitrogen', and 'residual non-protein nitrogen'. This latter consists largely of polypeptides, with traces of creatin, creatinin, urea, uric acid, purine bases, and pyrimidine bases. As regards estimations, Gunning's modification of Kjeldahl's method is used for the total nitrogen. Folin and Wu's method for the determination of non-protein nitrogen in blood has been found by the author to be satisfactory for the estimation of the non-protein of bacterial cultures. The 'formol' method is used for the determination of the free NH_2 groups, while the free NH_3 was done by the Folin-MacCollum modification of the Folin air-current method.

Five sets of tables are given. The first shows the composition of three samples of gelatin in terms of the six nitrogen fractions mentioned. It was found that the combined amino-nitrogen and NH_3-nitrogen comprise less than 10 per cent. of the total nitrogen. The second table shows the non-protein content (in milligrammes) of 100 c.cm. of a plain medium made up with a varying percentage of glucose. The third shows the amount of the various nitrogen fractions present in a control uninoculated medium, and in one containing seven-day cultures of *B. coli*. The fourth shows the effects produced by *B. proteus*—a much more energetic proteolytic bacterium. Here the amino-nitrogen fraction changes but little, although the free ammonia in the plain gelatin increases very much. The fifth table shows that the increase in free ammonia is due to the intracellular utilization of the protein for energy.

In the second paper the authors, by the above methods, have substantiated their previous findings, viz. the parallelism between ammonia formation in plain and glucose broth cultures during the earlier days of incubation. This stands in direct contrast to the other members of the dysentery group, which attack from the start the protein constituents of plain broth. From these they form progressive amounts of ammonia and produce coincidently a constantly increasing alkalinity. The same phenomenon is observed in cultures of staphylococci, and the explanation offered is that the carbohydrate moiety of the protein molecule is peculiarly vulnerable to the action of the Shiga bacillus and the staphylococcus. These microbes use the carbohydrate fraction, producing therefrom the acid and also sparing the nitrogenous constituents from attack until the carbohydrate is exhausted.

B. typhosus. Two strains were studied. Quantitative differences in the intensity of the reactions induced by these strains were clearly discernible, but the significance to be attached to them was not great.

B. paratyphosus α, grew well in both the plain and glucose gelatin, judging from the increase in the protein nitrogen fraction and the corresponding decrease in the non-protein constituents. Evidences of deamination, as shown by the free ammonia formation were absent in glucose gelatin, but that in plain gelatin showed a progressive increase.

B. paratyphosus β. A series of analytical tables is appended, showing that the nitrogenous metabolism of a culture of *B. paratyphosus β* is confirmatory of the general phenomena observed in cultures of *B. typhosus* and *B. paratyphosus α.*

The third paper deals with *B. coli.* In general, the nitrogenous changes produced are quantitatively similar to those found for *B. typhosus*, *B. dysenteriae*, and *B. paratyphosus.*

The protein nitrogen increase, indicative of the growth of the organisms with the transformation of some of the non-protein constituents of the medium into the actual bacterial substance, is not very different from that observed in cultures of the pathogenic members of the intestinal group. In other words, the rate of growth of all the microbes studied in this series is relatively about the same.

The Schmitz bacillus is studied in the fourth paper. Two cultures which were examined showed no signs indicative of the utilization of the carbohydrate portion of the protein molecule.

B. alkalescens brings about a rather vigorous change in reaction toward the alkaline side of neutrality in plain, sugar-free gelatin. Not only is there a considerable deamination and a distinct reduction in amino-nitrogen in the cultures after several days' incubation, but the reaction becomes decidedly alkaline.

B. proteus. Here the most striking change is that of the protein nitrogen fraction which, even within 24 hours of incubation, had diminished from 72 per cent. (that of the uninoculated control) to 53 per cent. in the glucose-free gelatin. This remarkable decrease in protein nitrogen is due to the activity of its proteolytic enzyme. There is coincidently a not inconsiderable increase in ammonia nitrogen.

In this case a further set of experiments was performed to determine what proportion of the decrease in protein nitrogen, and therefore what proportion of the increase in the polypeptide nitrogen, was due to the soluble enzyme of the bacteria, and what was due to the intracellular nitrogenous metabolism respectively. The carbol gelatin method of Kendall and Walker was used. It would appear that the significant change is due to the activity of the enzyme. W. A. M. S.

van Riemsdijk, M. Ueber einen neuen einfachen Sauerstoffindikator für die Züchtung von anaëroben Bakterien und die Kultur von Anaerobionten im allgemeinen. [**A new and simple oxygen indicator for the cultivation of anaerobic bacteria and the culture of anaerobes in general.**] *Centralbl. f. Bakteriol.*, Abt. I, 1922, Orig. **88**, 229.

The authoress has investigated the quantitative relations of caustic potash and pyrogallic acid in the absorption of oxygen, and finds that this is complete in 30 to 40 minutes in a vessel with a capacity of 400 c.cm. when 10 c·cm. of a 20 per cent. solution of KHO are mixed with 3 c.cm. of a 44 per cent. solution of pyrogallic acid. Instead of using solutions of methylene blue as an indicator of the disappearance of oxygen, she strongly recommends strips of hydrophil gauze which is impregnated with a solution of glucose and methylene blue constituted as follows:

3 c.cm. of 10 per cent. glucose.
1 drop nNaOH preserved in a brown dropping bottle.
1 drop of methylene blue (meth. blue Höchst 50 mgm. dissolved in dist. water 30 c.cm.).

An anaerobic culture apparatus recommended consists merely of a well-stoppered vessel containing the above-mentioned proportions of alkaline-pyrogallic acid, and is said to yield good results. W. B.

Gates, F. L. **Collodion sacs for aerobic and anaerobic bacterial cultivation.** *J. Exper. M.*, 1922, **35**, 635.

The author describes a convenient method for the preparation and use of collodion sacs for aerobic and anaerobic cultivations *in vitro*. Details of the technique should be consulted in the original. W. B.

Kairinkschtis, W. Neue statische Daten und Gesetzmässigkeiten aus der Pathologie des Tetanus. [**New statistical data and formulae in the pathology of tetanus.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1922, **95**, 220.

In a series of 444 cases of tetanus on the Russian front in the Great War the author was able to confirm previous experience with regard to the incubation period, site of trauma, and mortality. His figures show the localization of the injury greatly affects the length of the incubation, the latter being shorter the nearer the injury is to the central nervous system. With equal incubation periods death is postponed the farther the lesion is peripherally. For wounds of different regions the mortality of subsequent tetanus varied from 62·5 per cent. in the case of the hand to 80 per cent. in the case of the head. W. B.

Hall, I. C. **Differentiation and identification of the sporulating anaerobes.** [**B.**] *J. Infect. Dis.*, 1922, **30**, 445–504.

This is a long and careful study of the taxonomy of the obligate anaerobes based on the examination of 73 pure strains, all but 4 of which belong to 15 species. A new species, *B. centrosporogenes*, is described. The results generally are in close approximation with those found by Weinberg and Séguin, and by the Anaerobic Committee of the M. R. C. (1919). A differential diagnosis is given based on morphology, action on protein, and action on carbohydrates. The author considers that *B. cochlearius* is identical with *B. putrificus*, and on account of the priority of the latter the term *B. cochlearius* should be dropped. The author's new species, *B. centrosporogenes,* is a large Gram + rod with central spore formation in nearly all media. The rods are not swollen at the level of the spores. The vegetative rods are highly motile. Proteolysis is active. Coagulated egg albumin, brain, and meat media are digested and blackened. Gelatin is liquefied and blackened. Milk is coagulated and then liquefied. Glucose was fermented by all the 4 strains studied, but lactose, saccharose, salicin, glycerol, and inulin were left untouched. The microbe was non-pathogenic. The author believes that *B. centrosporogenes* has hitherto been confused in part with *B. bifermentans,* in part with central sporing *B. sporogenes.*

W. B.

Nasta. Contribution à l'étude de l'action du *B. histolyticus* sur les tissus. **[Contribution to the study of the action of *B. histolyticus* on the tissues.]** *Compt. rend. Soc. de biol.*, 1922, **87**, 279.

This is a study of the evolution of the lesions produced by the intramuscular inoculation by *B. histolyticus* on the guinea-pig. One-tenth of a c.cm. in glucose broth was the dose employed, the animals being killed at intervals of two hours. Even at the end of one hour there was an abundant gelatinous exudate with a slight ecchymosis. The author finds that the lesion is limited almost exclusively to the muscle fibres, which are transformed into a haemorrhagic mass and dissolved. The lysis of the muscle is due with certainty to a toxin secreted by the bacillus. W. B.

Kahn, M. C. A cultural study of anaerobic spore-bearing bacteria with strains isolated by the Barber single cell technic. *J. Med. Research*, 1922, **43**, 155.

The author has studied the morphological and biological characters of fifteen different anaerobic cultures which had been isolated from individual bacilli by the technique of Barber, and were therefore pure. He regards the vaseline-seal boiling method as the most reliable for obtaining anaerobiosis especially in liquid media. If the proper degree of anaerobiosis is established and maintained, anaerobic bacteria will grow well on relatively simple media if the P_H is adjusted to 7·2. The author finds that *B. welchii, B. tertius, B. fallax, V. septique,* and *B. oedematiens* are *non-proteolytic.* Those which attack proteins may be divided into two groups: (1) strongly proteolytic, including *B. sporogenes, B. botulinus, B. oedematis maligni,* Koch, and *B. histolyticus*; (2) feebly proteolytic, including *B. putrificus, B. tetani, B. bifermentans, B. bellonensis, B. aerofoetidus.* The reaction of the bacteria of the proteolytic types of media may in some instances be of specific differential value. The identification of a species within a group can only be made by studying the carbohydrate fermenting properties. Proteolytic activities of anaerobic bacteria are not lessened by the presence of fermentable carbohydrates. The author considers that the morphology of anaerobic spore bearers varies greatly with changes in environment and conditions of cultivation. Even when a constant medium and technique are employed, the morphology of any given micro-organism remains only fairly constant. The shape and appearance of colonies were not found to be a reliable basis for differentiation. W. B.

Freund, F. Ueber eine durch ein anaërobes Bakterium hervorgerufene Meningitis. [**Meningitis caused by an anaerobic bacterium.**] *Centralbl. f. Bakteriol.* (&c.), Abt. I, 1922, Orig. **88**, 9.

Case of a girl of 18 who died of meningitis following chronic ear disease. Fluid from the lateral ventricle revealed an anaerobic bacillus pathogenic for guinea-pigs and rabbits. The microbe was believed to be allied to, but not identical with, *B. funduliformis* described by Hallé.

W. B.

Berthelot, A., et **St. Danysz-Michel, Mme.** Sur la présence de microbes acétonogènes dans la flore intestinale des diabétiques. [**Acetone-forming organisms in the stools of diabetics.**] *Compt. rend. Acad. d. sc.*, 1922, **174**, 1303.

This is a preliminary note on certain researches of the authors on the presence of acetone-forming micro-organisms in the stools of diabetics. These micro-organisms were found in the stools of 17 out of 22 diabetics, and were not recovered once in those of 32 subjects who were either healthy or were suffering from some chronic disease other than diabetes. These micro-organisms have been of various types (bacillary, diplococcal, &c.). Experiments on rabbits over a period of several months have shown that these organisms, when ingested by mouth, are capable of producing glycosuria in rabbits fed on a diet rich in carbohydrates.

The authors disagree with Renshaw and Fairbrother (*Brit. M. J.*, 1922, i, 674), who have isolated an acetone-forming bacillus from the stools of diabetics, as to the causal relationship of these organisms with diabetes. They would rather explain the acetone-forming capacity of these organisms as an acquired characteristic due to their continuous growth in a medium unusually rich in carbohydrates, such as obtains in the lower alimentary tract of diabetics. J. R. P.

Fasiani, G. M. Ricerche eziologiche in un caso di Sodoku. [**Aetiological investigations in a case of rat-bite fever.**] *Riforma med.*, 1922, **38**, 293.

The present case is similar to those recently described by Mantovani (*Medical Science*, 1922, **6**, 145). *Spirochaeta morsus muris* was isolated after very laborious investigations and from one guinea-pig only out of many inoculated with blood from the patient. The short forms of spirochaeta described by Mantovani were not found. C. D. F.

Manouélian, Y. Recherches histomicrobiologiques sur la paralysie générale. Existence du tréponème dans le cytoplasme des cellules nerveuses de l'écorce cérébrale. [**Histological studies in G.P.I. Presence of *Treponema pallidum* in the nerve-cells of the cerebral cortex.**] *Compt. rend. Acad. d. sc.*, 1922, **174**, 1134.

This is a short note describing the presence of *Treponema pallidum* in the cytoplasm of cortical nerve-cells in G.P.I. J. R. P.

Warthin, A. S., and **Starry, A. C.** **The staining of spirochaetes in cover-glass smears by the silver-agar method.** *J. Infect. Dis.*, 1922, **30**, 592.

The authors describe a method of silver-impregnation applicable to the study of spirochaetes in smears, and they claim that it is the best method yet devised and should replace even the dark-ground method of diagnosis, Smears made on thin cover-slips are dried thoroughly in air and then fixed in absolute alcohol 3 to 5 minutes. Wash in distilled water. Rinse the cover-glass with smear in 2 per cent. silver nitrate and cover the smear side with a perfectly clean cover-glass also rinsed in the silver nitrate solution. Place the adherent pair of cover-glasses, so as not to separate them, in a bottle of 2 per cent. silver nitrate in an incubator for 1 to 2 hours, then remove the cover-glasses from the solution and separate them.

Place the cover-glass with the smeared side up in the following mixture:

2 per cent. silver nitrate solution	3·0 c.cm.
Warm 10 per cent. aqueous gelatin solution . .	5·0 „
Warm glycerol	5·0 „
Warm 1·5 per cent. agar suspension . . .	5·0 „
5 per cent. aqueous hydroquinone solution . .	2·0 „

After the solution is reduced, remove and rinse in 5 per cent. sodium thiosulphate solution. Wash in distilled water; clear in xylol and mount in balsam.

It is essential that all the ingredients should be pure. In successful preparations the spirochaetes appear black against a light background. It is often of advantage to clear the background by means of conc. hydrogen peroxide, which is best done after the alcohol fixation.

Smears stained by the above method are not always permanent, but they may be made so by toning for 5–15 minutes in a gold chloride solution having the following composition:

Ammonium sulphocyanide	6·25 gm.
Tartaric (or citric) acid	0·50 „
Sodium chloride	1·25 „
Distilled water	250 c.cm.
Gold chloride (1 per cent. solution) . .	6·25 „

Excellent illustrations accompany this paper. W. B.

Warthin, A. S. The excretion of *Spirochaeta pallida* through the kidneys. *J. Infect. Dis.*, 1922, **30**, 569.

By means of the Warthin-Starry silver-agar cover-glass method the author has examined three cases of congenital and two cases of acquired syphilis, and finds that there is a syphilitic spirochaeturia in the septicaemic stage of the infection. The spirochaetes may be excreted in enormous numbers through the convoluted tubules. During such excretion the spirochaete of syphilis suffers greater destruction than *S. icterohaemorrhagiae*, so that fewer organisms reach the urine in syphilis than in infectious jaundice. The author believes that spirochaeturia is more likely to occur when the spirochaetes in the blood-stream are exposed to the action of antibodies or spirochaeticides. The spirochaeturia appears to be associated with definite degenerative lesions of the epithelium of the convoluted tubules. The paper is illustrated by 23 admirable reproductions of microphotographs.
W. B.

Perkins, R. G., and **Spreng, D. S.** (1). **Organisms of *B. lactimorbi* group found in throat cultures and simulating *B. diphtheriae*.** *J. Infect. Dis.*, 1921, **29**, 513.

Perkins, R. G., and Shen, J. K. (2). Presence of *B. lactimorbi* in the throats of cats. *J. Infect. Dis.*, 1922, **30**, 505.

In the first of these papers the authors give a short account of *B. lactimorbi*—an organism found by Jordan and Harris (1909) in connexion with milk sickness. The interest of this micro-organism is its superficial resemblance to *B. diphtheriae.* It is, however, a motile sporing organism, which is Gram-negative. Polar staining is very marked, and the microbe may closely resemble the C type of diphtheria in Wesbrook's classification. It was found in rather less than 1 per cent. of throat cultures from suspected cases of diphtheria, and it was found to persist for long periods.

In the second paper the authors describe its occurrence in cultures taken from the throats of 7 cats out of a total of 25 examined. They think this may explain some of the alleged finding of *B. diphtheriae* in these animals. W. B.

Wilcox, Harriet L. The effect of peptone on the toxigenic property of *B. diphtheriae* No. 8. *J. Infect. Dis.*, 1922, **30**, 536.

An account of the degradation in toxigenesis shown by the famous Park-Williams No. 8 strain of *B. diphtheriae* and attributed to the influence of the peptone employed. W. B.

McIntosh, J., James, W. W., and Barlow, P. L. An investigation into the aetiology of dental caries. I. The nature of the destructive agent and the production of artificial caries. *Brit. J. Exper. Pathol.*, 1922, **3**, 138.

The examination of selected carious material showed the constant presence of a definite type of bacillus. The bacilli are capable of producing a high degree of acidity by the fermentation of carbohydrates. The average final P_H value of nine strains was 2·75, which is sufficient to decalcify teeth. Teeth left in contact with pure cultures over prolonged periods showed changes almost identical with those found in natural caries. Such teeth show erosion of the enamel with penetration of the dentinal tubules and the formation of liquefaction foci. The bacilli, to which it is proposed to give the name *B. acidophilus odontolyticus*, in their resistance to, and formation of, acid resemble the 'acidophilus' group of Moro; biologically, however, there are several points of difference. P. F.

Callender, G. R., and Coupal, J. F. An unusual case of nocardiosis. *J. Infect. Dis.*, 1922, **30**, 601.

The case is described of a physician, aged 53, who two years before his death inhaled a chicken vertebra into his right bronchus. Repeated X-ray examinations failed to reveal it. A few months later he had an attack of 'influenza' with pneumonia, and a similar attack a year later. After this his health failed and he was believed to be suffering from tubercle. Two weeks before his death he developed a right-sided hemiplegia and an abscess appeared in his leg. At autopsy a large lesion was found in his right lung with a cavity in the centre. The right inferior bronchus was thickened and dilated and surrounded a chicken's cervical vertebra. Abscesses were also found in the brain, and from them was obtained an anaerobic *Streptothrix* only slightly pathogenic for guinea-pigs. W. B.

Andriani, S. Contributo allo studio delle alterazioni istologiche del fegato e della milza nella lebbra. [**Contribution to the study of the histological changes of the liver and spleen in lepra.**] *Pathologica*, 1922, **14**, 221.

The author had the opportunity of carrying out his investigations in a case of tubercular leprosy, death having resulted from an intercurrent lobar pneumonia. The following changes were particularly noticed. In the liver, a greatly diffused process of hypertrophic cirrhosis with perihepatitis, perivascular infiltrations, and fatty degeneration of the liver-cells. In the spleen, intense sclerosis with splenomegaly, perisplenitis, disappearance of Malpighian follicles, rarefaction of lymphoid cells, and diffuse hyaline degeneration. The hepatic cirrhosis had in many places a distinctly insular character, but in others it was similar to the Laënnec type, which shows that in leprosy the hypertrophic and portal forms of cirrhosis may coexist. In both the liver and spleen many leprous cells and nodules were found. These were particularly numerous in the newly-formed connective tissue of the liver, from which they appeared to have spread to the parenchyma. A great number of bacilli were seen not only in the leprous cells but also in the hepatic and splenic tissues. In addition, the author noted the presence of many spherical bodies characterized by changing dimensions, homogeneous aspect, and basophil reaction. The micro-chemical investigations carried out for their identification lead the author to the conclusion that they were essentially formed of an incompletely differentiated hyaline substance and that they probably originated from a degeneration of old plasma cells. C. D. F.

Selter, H. Über die Wirkung abgetöteter Tuberkelbacillen. [**On the action of killed tubercle bacilli.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1922, **95**, 233.

This paper contains the protocols of experiments on guinea-pigs treated with different preparations of killed or extracted tubercle bacilli. Inoculations of such are powerless to induce an immunity to living tubercle bacilli subsequently injected. The author utilized in these experiments Much's lactic acid extracted T.B. ('M.T.B.') as well as a 'vital tuberculin' prepared by himself from crushed tubercle bacilli. W. B.

Bosworth, A. W., Elkins, Marion G., and **Blanchard, Marguerite E. A study of ammonia production by a certain strain of avirulent human tubercle bacillus.** *J. Infect. Dis.*, 1922, **30**, 357.

During a growth of six weeks an avirulent culture of human tubercle bacilli showed continuous production of ammonia in plain, dextrose, mannitol, and glycerol broths. Over 30 per cent. of the nitrogen present in the medium may be converted into ammonia which is partly retained in the medium although the greater part is lost by volatilization. W. B.

Würtzen, C. H., e **Holten, C.** Om Bevægelsers Indflydelse paa Temperaturen, særlig hos Tuberkulöse. [**The influence of exercise on the temperature, notably in the tuberculous.**] *Hosp.-Tid.*, 1922, **65**, 101–13, 133–53.

Würtzen and Holten have taken the rectal temperatures of 130 persons, 20 of whom were healthy convicts. All the tuberculous persons were afebrile, although as many as 60 were in the third stage of pulmonary tuberculosis. Every person rested for 2 hours, after which the temperature was taken. Then the person walked slowly on the flat for 15 minutes, at the end of which time the temperature was again taken. If it was raised, the temperature was taken every 5 minutes until it had fallen to the temperature before the walk. The same experiment was repeated with 10- and 5-minute walks respectively. The chief result of these investigations was the finding that there is little difference in the reaction of healthy and tuberculous persons to mild exercise, and that in one and the same healthy person the same exercise may provoke very different temperature reactions from time to time. One day a rise of 1·1° C. may be observed, another day the rise may be only 0·1° C. in the same person. The rate at which the exercise temperature falls may also vary greatly from day to day in the same person. Some healthy persons invariably show a rise of temperature after 15 minutes' walk, but not after 10 minutes', while others never show such a rise. The investigators, who are sanatorium physicians, had hoped to find a normal standard of temperature reaction to exercise in healthy persons with which the temperature reaction of tuberculous persons could be compared. But, as their 12 elaborate tables show, there is practically no demonstrable threshold between health and disease in this respect. Tuberculous persons do, indeed, develop a rise of temperature after slight exertion more often than healthy persons, but the exceptions are too frequent in both classes to render this distinction valuable. In one and the same person, whether he be healthy or tuberculous, the time taken for an exercise temperature to fall to normal may be 40 minutes on one occasion and only 5 on another. In 13 out of the 20 healthy 'controls' there was actually a fall of temperature after exercise; some of the tuberculous persons showed the same phenomenon. C. L.

Kleinschmidt, H. Gibt es Phlyktänen ohne Tuberkuloseinfektion? [**Can phlyctenules exist without tuberculous infection?**] *Beitr. z. Klin. d. Tuberk.*, 1921, **48**, 188–94.

Kleinschmidt answers in the affirmative the question: Can phlyctenules exist without tuberculous infection? At the University Childrens' Hospital in Hamburg he has observed, in the course of a year, 5 children who suffered from definite phlyctenular conjunctivitis and who gave a negative cutaneous reaction to tuberculin. Four of the children were about the age of 2, the fifth was 3 years old. In no case had they been in contact with tuberculosis, but 1 child suffered from pyelitis, another from congenital syphilis, and 2 from rickets. Only in 1 case was there a severe degree of exudative diathesis. In every case the conjunctivitis was comparatively slight, and in 4 only one eye was affected. Under treatment with yellow ointment the disease cleared up in a few days, but short relapses occurred on 2 occasions. Kleinschmidt refers to Czerny's teaching, according to which phlyctenular ophthalmia depends on two factors, the one being endogenous, a constitutional anomaly, such as the exudative diathesis, the other being an exogenous poison, the most common of which is the tubercle bacillus. Less common are the poisons of measles and other diseases.

C. L.

Pane, N. Un metodo semplice per la dimostrazione microscopica di bacilli tubercolari in espettorati a reperto difficile o negativo. [**Simple method for the demonstration of tubercle bacilli in expectorations with few or apparently no bacilli.**] *Riforma med.*, 1922, **38**, 313.

The expectoration is collected in a sterile Petri dish or glass box with four times its volume of sterile physiological solution, and put for 24 hours in an incubator at 37° C. By that time the mucus and cells are rendered fluid by the proteolytic enzymes elaborated by bacteria contained in changing quantity in any sputum, and it is then only necessary to centrifuge the fluid and make preparations from the sediment in the usual way. According to the author the results are more reliable than by the antiformin method, which is, in his opinion, likely to alter tubercle bacilli. C. D. F.

Maië, Shin. Experimentelle Versuche bei Goldfischen (*Carassius auratus*) mit säurefesten Bazillen. [**Experiments on goldfish (*Carassius auratus*) with acid-fast bacilli.**] *Centralbl. f. Bakteriol.* (&c.), Abt. I, 1922, Orig. **88**, 28.

Record of experiments on goldfish inoculated with fish tubercle bacilli, acid-fast bacilli isolated from water, and *B. leprae.* In a large number of control goldfish acid-fast bacilli could not be found in the organs although many acid-fast bacilli were found in the intestines. These were, however, not pathogenic for goldfish. *B. fluorescens* isolated from the intestine was found to be highly virulent for other goldfish. Experiments with fish T.B. showed that goldfish are susceptible, and that the principal lesions were found in the kidneys. Acid-fast bacilli (*Mycobacterium aquae*, Galli-Valerio) isolated from water were also found to be pathogenic for goldfish, although they usually underwent an extensive extracellular bacteriolysis. Leprous nasal secretion or leprous nodules inoculated into goldfish, intraperitoneal, intracerebral, or intramuscular, frequently spread into the kidneys, but in general the leprosy bacilli were not capable of multiplying. W. B.

Swift, H. F., Boots, R. H., and **Miller, C. P., jun. A cutaneous nematode infection in monkeys.** *J. Exper. M.*, 1922, **35**, 599.

While attempting to reproduce rheumatic fever in monkeys (*Macacus rhesus*) subcutaneous nodules, joint swellings, and fever were observed, and were at first believed to be connected with rheumatism, as they had developed after inoculation of material from cases of rheumatic fever. It was subsequently found that similar lesions were present in uninoculated animals, and they were found, in fact, to be due to an infection with a hitherto undescribed nematode to which the name *Trichosoma cutaneum* has been given provisionally. In the subcutaneous nodules larval forms of the worm and possibly adult males were found. The reaction round the parasites consisted of proliferation of fixed cells and invasion of eosinophils, with subsequent presence of giant cells, newly-formed vessels, and capsule formation. The adult female burrows in the epidermis, producing an elongated serpiginous blood-blister which becomes purulent. In this blister the eggs are laid, and by its rupture they are discharged and infect the new host. The paper is illustrated with admirable photographs. W. B.

Gins, H. A. Untersuchungen über die für Variola und Vaccine spezifischen Zellveränderungen. [**Researches on the cell changes which are specific for variola and vaccinia.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1922, **95**, 255.

This is a reinvestigation into the nature of the much discussed Guarnieri's cell inclusions of the rabbit's cornea when infected with variola or vaccinia. The majority of writers since Hückel's publication in 1898 have regarded them as degenerative. The present author considers that they are independent bodies, foreign to the cells, and occurring not only in, but also between, the cells of the cornea. They may, in his opinion, represent forms in the development of the variola or vaccinia virus. He conceives that the virus penetrates into the cells and wanders into the nucleus and increases in size there, ultimately filling the whole nucleus. The bodies then disappear from the nucleus and grow in the cells, which present a radiate-like arrangement (' Strahlzelle '), ultimately appearing outside the cell altogether as vaccine ' bodies '. These bodies, penetrating into the cells, cause the Guarnieri appearance, and after maturation break up into elementary bodies which are probably those described by Paschen.

W. B.

Levaditi, C., et **Harvier, P.** (1). Premières recherches sur le virus de l'encéphalite léthargique. [**First studies of the virus of *Encephalitis lethargica.***] *J. méd. franç.*, 1920, **9**, 121–4.

Levaditi, C., et **Harvier, P.** (2). Recherches expérimentales sur le virus de l'encéphalite léthargique (encéphalite épidémique). [**Experimental studies of the virus of *Encephalitis lethargica.***] *Bull. Acad. de méd.*, 1920, **83**, 365–7.

Harvier, P., et **Levaditi, C.** (1). Recherches sur l'encéphalite léthargique. [**Experimental studies of *Encephalitis lethargica.***] *Bull. et mém. Soc. méd. d. hôp. de Par.*, 1920, **44**, 179–85.

Harvier, P., et **Levaditi, C.** (2). Preuve anatomique et expérimentale de l'identité de nature entre certaines chorées graves aiguës fébriles et l'encéphalite léthargique. [**Anatomical and experimental proof of the identity between certain forms of *Chorea gravis* and *Encephalitis lethargica.***] *Bull. et mém. Soc. méd. d. hôp. de Par.*, 1920, **44**, 583–8.

Harvier, P., et **Levaditi, C.** (3). Virulence des centres nerveux dans l'encéphalite six mois après le début de la maladie. Virus encéphalitiques atténués. [**Virulence of the central nervous system in *Encephalitis lethargica* six months after the onset. Attenuated forms of the virus.**] *Bull. et mém. Soc. méd. d. hôp. de Par.*, 1920, **44**, 1487–90.

Harvier, P. Les recherches expérimentales sur l'encéphalite aiguë épidémique. [**Experimental studies of *Encephalitis lethargica.***] *Rev. de méd.*, 1920, **37**, 353–8.

Levaditi, C., et **Harvier, P.** (1). Étude expérimentale de l'encéphalite dite léthargique. [**Experimental study of *Encephalitis lethargica.***] *Ann. de l'Inst. Pasteur*, 1920, **34**, 911–72.

Levaditi, C., et **Harvier, P.** (2). Recherches expérimentales sur le virus de l'encéphalite léthargique (encéphalite épidémique). [**Experimental studies of the virus of *Encephalitis lethargica.***] *Compt. rend. Soc. de biol.*, 1920, **83**, 385.

Levaditi, C., et **Harvier, P.** (3). Recherches expérimentales sur l'encéphalite léthargique. [**Experimental studies in *Encephalitis lethargica.***] *Compt. rend. Soc. de biol.*, 1920, **83**, 674.

Levaditi, C., et **Harvier, P.** (4). Recherches sur le virus de l'encéphalite épidémique. [**Studies of the virus of *Encephalitis lethargica.***] *Compt. rend. Soc. de biol.*, 1920, **83**, 1140–2.

Levaditi, C., et **Harvier, P.** (5). Recherches expérimentales sur l'encéphalite épidémique. [**Experimental studies in *Encephalitis lethargica.***] *Compt. rend. Soc. de biol.*, 1921, **84**, 300–3.

Levaditi, C., Harvier, P., et Nicolau, S. (1). Recherches expérimentales sur le virus de l'encéphalite épidémique. [**Experimental studies of the virus of *Encephalitis lethargica*.**] *Compt. rend. Soc. de biol.*, 1921, **84**, 524–7.

Levaditi, C., Harvier, P., et Nicolau, S. (2). Sur la présence dans la salive des sujets sains d'un virus produisant la kérato-conjonctivite et l'encéphalite chez le lapin. [**The presence in the saliva of the healthy subject of a virus capable of producing a keratitis and an encephalitis in the rabbit.**] *Compt. rend. Soc. de biol.*, 1921, **84**, 817.

Levaditi, C., Harvier, P., et Nicolau, S. (3). Transmission expérimentale du virus de l'encéphalite de la mère au fœtus. [**Experimental transmission of the virus of *Encephalitis lethargica* from the mother to the fœtus.**] *Compt. rend. Soc. de biol.*, 1921, **84**, 957–9.

Levaditi, C., Harvier, P., et Nicolau, S. (4). L'affinité cutanée du virus encéphalitique. [**Cutaneous affinity of the virus of *Encephalitis lethargica*.**] *Compt. rend. Soc. de biol.*, 1921, **85**, 287.

Harvier, P. Les virus filtrants neurotropes. [**Neurotropic filter-passing viruses.**] *Paris méd.*, 1921, **11**, 485–93.

Levaditi, C. (1). Étude expérimentale de l'encéphalite léthargique. [**Experimental study of *Encephalitis lethargica*.**] *Bull. de l'Inst. Pasteur*, 1921, **19**, 289–304, 337–48.

Levaditi, C. (2). Les feuillets embryonnaires en rapport avec les microorganismes pathogènes. [**Embryonic layers and their relation to pathogenic microorganisms.**] *Compt. rend. Acad. d. sc.*, 1921, **173**, 370–794.

Levaditi, C., Harvier, P., et Nicolau, S. Étude expérimentale de l'encéphalite dite 'léthargique'. (Deuxième mémoire.) [**Experimental study of *Encephalitis lethargica*.**] *Ann. de l'Inst. Pasteur*, 1922, **36**, 61–148.

In the course of their researches into the virus of encephalitis lethargica, Levaditi and his co-workers have made a series of communications to various scientific bodies, but their main conclusions up to date have been collected in two outstanding papers, Nos. 17 and 19 of the above list of references.

Susceptibility of animals and modes of infection. Great difficulty was encountered at first in transmitting the disease to animals. Out of 30 inoculations of material obtained from human cases of encephalitis lethargica into monkeys, rabbits, and guinea-pigs, two positive results only were obtained. In both cases rabbits were the animals employed, and the central nervous system of fatal cases of the disease was the material injected. Once a successful passage had been obtained in the rabbit no difficulty was encountered in passing the disease to rabbits, guinea-pigs, and mice, but monkeys show much natural immunity even to the fixed virus. In their earlier experiments the authors employed chiefly the intracerebral route, but subsequently the nasal, and especially the ocular, routes have been used in the majority of cases. With a virus which had undergone a large number of passages in rabbits it was found possible to transfer the disease to rabbits by inoculation into the testicle, intramuscularly, intraperitoneally, and intratracheally, as well as by injection into the sheath of a peripheral nerve and by dermal scarification. In the case of mice it is also possible to transmit the disease by subcutaneous inoculation.

The intravenous, subcutaneous, and alimentary routes, as well as injections into the salivary glands, have proved negative in rabbits.

In the case of the intranasal and ocular routes it is a necessary preliminary to damage the mucous membrane to obtain a positive result. Simple scarification of the cornea or injection into the anterior chamber of the eye also confer the disease on rabbits in the majority of cases. The only route which yields an invariably positive result is the intracerebral one.

In the case of the corneal route a keratitis is one of the first symptoms of a successful passage, and in the majority of cases the rabbit dies of an encephalitis in 7–13 days, but longer periods up to 3 weeks are occasionally encountered—for instance, after an intraperitoneal injection of the virus. If the animal is under the influence of an hypnotic at the time of inoculation, and for a little while after, the period of incubation is shortened by the various routes.

Resistance of the virus to various bactericidal agents. Exposure to a temperature of 55° to 70° C. kills the virus. The action of 1 per cent. carbolic acid in saline on the virus kills it in 3 days, but not in 15 minutes. Desiccation over H_2SO_4 and *in vacuo* does not kill the virus even after 44 days. Bile and various dyes (e. g. methylene blue) kill the virus very quickly.

Nature and mode of preservation of the virus. The virus of encephalitis lethargica is ultramicroscopic, and attempts at cultivation have proved unsuccessful. It is preserved as virulent brain substance obtained from animals which have died of the disease. It is best preserved in glycerine, either pure or diluted up to 1 in 3 of normal saline. It remains alive in milk for 96 days in the ice-chest or in water for a fortnight.

An emulsion of virulent brain in normal saline is still capable of conferring the disease on rabbits at a dilution of 1 in 1,000. The filtrate of an emulsion of virulent brain through Chamberland candles Nos. 1 and 3 is capable of transmitting the disease, but the micro-organisms which are arrested by these candles are not stated.

Sources of the virus. Apart from the central nervous system the only other source of the virus in the case of the above investigators has been the nasopharyngeal secretion of human cases of encephalitis lethargica. In the case of animals which have died of the disease, the virus has only been recovered from the central nervous system or from the site of inoculation. Contrary to the findings of Strauss, Hirshfeld, and Loewe (*N. York M. J.*, 1919, **109**, 772), the virus has not been recovered from the cerebrospinal fluid, and also, contrary to the findings of Netter, Césari, and Durand (*Compt. rend. Soc. de biol.*, 1921, **84**, 854), it was not recovered from the salivary glands of animals which had died of the disease. The authors also failed to find the virus in the lymphatic glands, blood, and spinal ganglia of infected rabbits, the last (spinal ganglia) being particularly interesting as they are virulent in experimental rabies and poliomyelitis. On the other hand, the present authors have obtained a virus similar to that of encephalitis lethargica, though in an attenuated form, from the saliva of healthy persons, presumed, therefore, to be carriers of the virus. The unfiltered saliva of these persons, when inoculated into the cornea of a rabbit, produces a keratitis followed by an encephalitis transmissible in series.

In a more attenuated form a virus capable of producing a keratitis, but not an encephalitis, in the rabbit can be obtained from the saliva of healthy persons (2 out of 13). This last virus dies after a few passages.

When the first series of experiments under review was published, Blanc (*Compt. rend. Acad. d. sc.*, 1921, **172**, 725) drew attention to the similarity of the results obtained by Levaditi and his co-workers with the virus of encephalitis lethargica on the one hand and those obtained by themselves, Doerr, and others with the virus of herpes. Levaditi then conducted a similar series of experiments with the latter virus, and came to the conclusion that the two viruses are identical, though behaving differently in man according to whether it is met with at a time of an epidemic (E. L.) or sporadically (herpes). The virus of herpes shows a greater affinity for the skin and that of encephalitis lethargica for the central nervous system, and the former is only an attenuated form of the latter.

Immunity: (1) *Acquired.* A subcutaneous inoculation with the killed or living virus does not protect a rabbit against a subsequent intracerebral inoculation of the living virus, but previous subcutaneous vaccination with the living virus protects the animal against a corneal inoculation (i.e. no keratitis develops) and vaccination with the killed virus produces only a partial immunity against a subsequent corneal or intranasal inoculation.

The blood-serum of a rabbit immunized as above fails to neutralize the virus *in vitro.* The blood-serum of a human case of encephalitis lethargica is capable of partially neutralizing the virus *in vitro* several months after the onset of the disease, but not earlier. The cornea of a rabbit which has recovered from a keratitis produced by the virus of herpes or by that obtained from normal saliva is immune to a subsequent inoculation of the fixed virus, but the other cornea is not. A rabbit which has recovered from an experimental keratitis of this type is sometimes immune to a subsequent intracerebral inoculation, but is not immune to a cutaneous inoculation, as herpetic vesicles will develop at the point of inoculation.

(2) *Natural.* The blood-serum of animals which are naturally immune to the virus of encephalitis lethargica (e.g. monkeys) fails to neutralize the virus *in vitro.*

Spontaneous infection was noticed once only in the case of a rabbit placed in a cage which had previously harboured infected animals.

Experimental transmission of the disease from the mother to the foetus has been realized, the virus being recovered from the brain and the breasts of the mother, the placenta, and the brain of the foetus.

The authors have also carried out some experiments with the viruses of rabies, vaccinia, and poliomyelitis, and divide the various viruses studied according to their affinity for the dermal or nervous tissues, as follows:

	Virus.	Affinity for			
		Skin.	Cornea.	Brain.	Spinal Cord.
Encephalitic Group.	1. Herpes (other than zoster) 2. From normal saliva (very attenuated)	+	+	±	−
	3. From saliva of healthy carriers 4. Encephalitis lethargica	+	+	+	±
	5. Vaccinia	+	+	±	±
	6. Rabies	−	±	+	+
	7. Poliomyelitis	−	−	−	+

The authors group these various viruses together under the term 'Ultra-virus neurotropes', and the affections they give rise to under the term 'ectodermoses', and point out that the tissues affected are all derived from the ectoderm of the embryo. They would also group the various diseases caused by bacteria under the term 'mésodermoses', i.e. affections mostly of tissues derived from the mesoblast.

Histology. The authors confirm the main histological findings so far recorded in encephalitis lethargica. The following are the principal points they have noted in experimental encephalitis:

1. The so-called encephalitis is really a meningo-encephalitis, the meningeal exudate being characterized by an almost complete absence of polymorphs, only lymphocytes and a few plasma cells being seen—an important point in differential diagnosis.
2. The encephalitis proper, on the other hand, shows the presence of a large number of polymorphs, especially in animals which have died in 2–3 days after infection; in such animals the polymorph is sometimes the predominating cell present.
3. The cornu ammonis is the site of election as far as maximal histological changes are concerned.
4. The authors describe cellular inclusions in the nerve-cells of the elective zone, and of that zone only, in 13 per cent. of the animals examined. These inclusions are similar to those described by Da Fano as 'minute bodies' in human cases of encephalitis lethargica, but the intracellular distribution is different in the experimental animal in that they are mostly intranuclear or, at any rate, closely adherent to the nuclear membrane. These bodies are surrounded by a clear halo like Da Fano's, and can be demonstrated by various stains such as Mann's, Unna's polychrome blue, &c. The authors' suggestion in regard to the nature of these cellular inclusions is that they are an acidophilous degeneration of the nucleolus acted on by the virus of encephalitis lethargica. J. R. P.

Vegni, R. Contributo allo studio sperimentale dell' infezione erpetica. [**Contribution to the experimental study of herpetic infection.**] *Riforma med.*, 1922, **38**, 270.

Confirmation of the results obtained by previous authors. 82 per cent. of the animals successfully inoculated through the corneal route died of herpetic encephalitis. The virus thus obtained was found to be virulent for the rabbit and guinea-pig, this last animal being perhaps more sensitive than the rabbit to subdural inoculations. According to the author, the herpetic virus loses its keratogenous properties when warmed for one hour at 50° C., but it is virulent if inoculated subdurally. In his opinion the virus is a filter-passer, but no mention is made of the kind of filter used. In the nerve-cells of the Ammon's horn of successfully inoculated animals intracellular bodies and granules of changing size were seen, but the author was not able to form any definite opinion as to their nature. C. D. F.

Plotz, H. Contribution à l'étude de la culture *in vitro* du virus de la vaccine. [**Cultivation *in vitro* of the virus of vaccinia.**] *Compt. rend. Acad. d. sc.*, 1922, **174**, 1265.

The author claims to have grown the virus of vaccinia *in vitro* by using the following technique: A rabbit is inoculated with vaccine lymph in the skin of the abdomen and is bled 3 to 4 days later. 2 to 3 c.cm. of its blood-serum are introduced into test-tubes containing glucose broth (1 per cent. glucose) and a piece of fresh kidney (Smith-Noguchi method).

A layer of liquid paraffin renders the medium anaërobic and the latter is incubated at 39–40° C. For subcultures the medium is altered to the extent of having some fresh normal rabbit's serum added in the proportion of 1 to 3. On incubation the medium becomes cloudy, and after 4 to 5 days a white precipitate forms on standing at room-temperature. A microscopical examination of the deposit reveals the presence of minute coccoid bodies measuring from 0·2 to 0·3 μ in diameter.

Subcultures have been carried as far as 14 generations. The typical lesions of vaccinia are reproduced by the 10th generation (the latest tested) though in a somewhat milder form. J. R. P.

Cantani, A. Immunizzazione antitubercolinica rapida con tubercoline iodizzate e risultati terapeutici. [**Rapid antituberculinic immunization with iodized tuberculins and therapeutic results.**] *Riforma med.*, 1922, **38**, 265.

Experiments were made in man by means of mixtures of solutions of iodine in glycerol and tuberculin. The proportions were such that the quantity of iodine was from twice to ten times greater than that of tuberculin. For successive injections mixtures were used containing progressively diminishing quantities of iodine and progressively increasing quantities of tuberculin. The conclusions reached are: by means of iodized tuberculins it is possible to obtain in tuberculous subjects a rapid and intense antituberculinic immunization. This is proved by the presence in the blood of great quantities of specific antibodies, and by the fact that in the immunized subjects all tuberculinic reactions remain negative. However, one cannot at present state that the treatment has a favourable influence on the course of the disease. C. D. F.

Durand, F. La vaccinazione con i germi associati della tubercolosi polmonare. [**On vaccination with associated germs of pulmonary tuberculosis.**] *Riforma med.*, 1922, **38**, 173.

Vaccination with the associated germs of pulmonary tuberculosis appears to have a beneficial influence on the general condition of the patients and perhaps on the course of the disease itself. It is advisable to use killed germs at first and then attenuated ones in slowly progressing quantities. The germs may be obtained either directly from the patients by the Koch-Kitasato method or from the expectoration. Preventive vaccination of subjects in the initial stage of the malady with germs obtained from other patients is recommended. C. D. F.

Versari, A. Le reazioni di Von Dungern e di Gaté e Papacostas nella sifilide. [**The reactions of von Dungern and Gaté and Papacostas in syphilis.**] *Riforma med.*, 1922, **38**, 175.

According to the author, in secondary syphilis von Dungern's indigo test and Gaté and Papacostas' formalin reaction give a percentage of positive results smaller than that observed by Wassermann's test. In the later stages of the disease the contrary result is obtained. C. D. F.

Paxson, W. H., and **Redowitz, E.** ***Bacillus diphtheriae*; immunological types; toxin-antitoxin relationship.** *J. Immunol.*, 1922, **7**, 69.

In 1920 Havens distinguished two distinct agglutinogenic groups of *B. diphtheriae*, 82 per cent. of the total falling in one group and 18 per cent.

in the other. He prepared toxins from each group and found that their neutralization by diphtheria antitoxin was complete in Group I and partial or incomplete in Group II. The present authors have re-examined this question on seven strains of diphtheria bacilli, and, although they were able to separate them agglutinogenically, they were unable to confirm Havens's contention that the toxins in Group II, were not neutralized by standard antitoxin to the same extent as those of Group I. One, one and a half, and two units of standard antitoxin injected simultaneously with large doses of virulent cultures protected guinea-pigs against both types of *B. diphtheriae.*
W. B.

Selter, H. Die Immunitätsverhältnisse bei Meerschweinchentuberculose. [**Immunity relations in tuberculosis of guinea-pigs.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1922, **95**, 159.

This is an elaborate experimental research in which guinea-pigs were inoculated with a culture of tubercle bacilli the virulence of which was such that 50 bacilli caused definite visceral tuberculosis in 3 to 5 months. The object of the work was to see whether an immunity was established as the result of a slow chronic tuberculosis. This was, in fact, found to be the case, provided that the subsequent reinfection was not too severe. Big reinfecting doses caused only a local reaction without influencing deleteriously the already developed visceral tuberculosis. If the result of the first dose was negative the animals reacted like the controls when the reinfecting dose was applied. W. B.

D'Aunoy, R. Antibody production after intratracheal injection of antigen. *J. Infect. Dis.*, 1922, **30**, 347.

Antibody formation after intratracheal injection of antigen was studied in rabbits and guinea-pigs and was found to take place in the same way as after injection—subcutaneous, intraperitoneally, or intravenously. In the case of lysins for human and sheep erythrocytes the formation was slower than after intravenous injection, whereas bacteriolysins for *V. cholerae* were elaborated earlier and in larger quantities than when the intraperitoneal route was employed. W. B.

Hirsch, E. F., and **Peters, Ebba C. Hydrogen-ion studies. II. Changes in the reaction of serum on thermal destruction of complement.** *J. Infect. Dis.*, 1922, **30**, 263.

By means of the gas-chain method the authors have studied the changes in the H-ion concentration of normal guinea-pig and rabbit serum after it has been heated to 56° C. in the process of inactivation. There is a prompt change in the reaction which is attributed to a dissociation of the complement substance or substances. W. B.

Hirsch, E. F., and **Williams, J. L. Hydrogen-ion studies. I. Changes in the reaction of the blood during anaphylactic shock.** *J. Infect. Dis.*, 1922, **30**, 259.

The authors have studied the changes in the reaction of the blood during anaphylactic shock in rabbits sensitized by intraperitoneal injections of sheep serum, human serum, sheep corpuscles, or egg white. There is a diminished alkalinity of the blood varying apparently with the severity of the symptoms. The change in reaction may be so great as to be incompatible with life. Along with the altered reaction of the blood there is a lowering of the alkali reserve. Slight changes may also occur in the concentration of the blood-sugar. W. B.

Kanai, S. Further experimental studies of immunization against *B. dysenteriae* (Shiga) and its toxins. *Brit. J. Exper. Pathol.*, 1922, **3**, 158.

The toxin of *B. dysenteriae* (Shiga) affects principally the central nervous system (medulla and spinal cord) in rabbits. At the same time it acts upon the capillary circulation generally, with the production of congestion and haemorrhage in the various viscera. Exposure to a temperature of 80° C. for one hour markedly reduces its toxicity, especially for the central nervous system. It has been impossible to effect a separation between exotoxin and so-called endotoxin on the lines of Olitsky and Kligler. Though there is some indication in the foregoing experiments that oral immunization produces a local immunity in the intestinal wall, this point remains undecided. The oral administration of the Shiga vaccine gives rise to less general reaction than does its inoculation subcutaneously. The antibody titre of the serum of rabbits immunized *per os* is appreciably raised by repeated ingestions. Attempts to secure, by subcutaneous and oral administration of killed vaccines, a solid active immunity against the potent soluble toxin of *B. dysenteriae* (Shiga), intravenously administered, have not been attended with the striking success realized in previous work, when active immunity was sought to the live bacilli similarly administered. Consequently, comparative estimates of the value of oral and subcutaneous methods in this connexion are not at present possible. P. F.

Dyke, S. C. On isohaemagglutination. *Brit. J. Exper. Pathol.*, 1922, **3**, 146.

Absorption tests performed on sera of Groups II, III, and IV, using corpuscles of Groups I, II, and III, confirm von Dungern and Hirschfeldt's hypothesis as to the distribution and nature of agglutinins and agglutinable factors in the four blood groups.

Sera from different individuals of the same group vary in their agglutinating powers. The relative titre of the two agglutinins in any given Group IV serum may be equal or very unequal. Sera from different individuals of this group differ greatly in this respect. Corpuscles from different individuals of the same group vary as to their agglutinability by the same serum. The relative degree to which the agglutinable factors may be present in corpuscles from any individual belonging to Group I varies greatly; corpuscles from different individuals belonging to Group I differ in this respect. P. F.

Hayden, A. F. The relative value of human and guinea-pig complement in the Wassermann reaction. *Brit. J. Exper. Pathol.*, 1922, **3**, 151.

There is for practical purposes a constant ratio between the haemolytic titre of healthy human complement and the capacity for being fixed with syphilitic antigen and antibody. Among 44 individuals tested the variation did not exceed 1 m.h.d. The fixation of human complement is quantitatively greater than that of the guinea-pig, a difference of from 2 to 3 m.h.d. being usual, and as much as 5 m.h.d. not uncommon. It is probable that active serum methods owe their greater delicacy to this factor and not to inactivation of the serum. P. F.

Callow, Bessie R. Bacteriophage phenomena with *Staphylococcus aureus*. *J. Infect. Dis.*, 1922, **30**, 643.

The authoress demonstrated the presence of a 'bacteriophage' principle, transmissible in series in the pus of sixteen staphylomycoses. In two of these the lytic principle was active against the homologous as well as against heterologous strains of staphylococcus. In six others it was lytic for heterologous but not for the homologous strain. W. B.

Fleming, A. On a remarkable bacteriolytic element found in tissues and secretions. *Proc. Roy. Soc.*, 1922, B. **93**, 306.

In the course of an investigation into the aetiology of a case of nasal catarrh, the author isolated a certain micrococcus to which he gave the name *M. lysodeikticus*. This micrococcus was observed to be completely inhibited in growth by nasal mucus from the patient, and, further, if a drop of nasal mucus was added to a thick suspension of the coccus, complete solution took place in a few minutes at 37° C. Subsequently, it was found that most tissues and secretions of the human body and some animal and vegetable tissues, especially egg white, had a powerful inhibitory and lytic action upon this coccus. This lytic substance is described as a 'lysozyme'.

The potency of the bactericidal action may be shown by treating a thick suspension of *M. lysodeikticus* with tears in a dilution of 1 in 9,000. The whole of the cocci were destroyed, and even up to 1 in 243,000 of tears there was a marked bactericidal effect.

The lytic action of lysozyme is extraordinarily rapid. At 45° C. a 1 in 5 dilution of egg white will completely dissolve a very thick suspension of *M. lysodeikticus* in 10 seconds; or a drop of tears allowed to fall upon a heavily-grown plate culture will, at room temperature, entirely remove the growth from the circle involved in 10 minutes.

With regard to the physical properties of lysozyme, it was found to be soluble in water but not in chloroform, ether, &c. These latter substances were found not to injure the lysozyme, and therefore can be used to preserve it. Desiccation has no effect, and commercial egg albumin is rich in lysozyme. The substance is precipitated with proteins and is extremely sensitive to slight alterations in the reaction of the medium, either to the acid side of neutrality or to the alkaline. There is no sharp thermal death-point, but activity begins to fail above 60° C.; at 75° C. it is seriously affected, and at 100° C. only traces are left. The heat resistance was found to be the same as that of ptyalin. Lysozyme is totally absorbed from solutions by porcelain filters, cotton wool, or filter-paper, but after these are saturated the solution comes through in undiminished strength.

Lysozyme exists in nearly all tissues of the body, especially epidermal structures (hair), the lining of the respiratory tract, and connective tissues (fibrous, fatty, or cartilaginous). It is also present in most body-fluids, but not in normal urine, cerebrospinal fluid, or sweat.

Lysozyme is not, however, confined to the human body; other animals' tissues contain it, but not to such a marked extent. For instance, rabbit or guinea-pig tears have no effect. In the vegetable kingdom turnip, only, is found to give a positive result.

The author then carried out experiments to find to what extent other bacteria than *M. lysodeikticus* were affected, and concluded that, in general, bacteria from the air (104 strains) were much more frequently destroyed than pathogenic bacteria; in fact, the only bacteria pathogenic to man which were frequently attacked were streptococci and staphylococci.

The author points out that the function of tears, saliva, and nasal secretion may not be, as thought, to wash bacteria away, but to destroy them. Air microbes are non-pathogenic to man, and they could hardly be otherwise in face of the lysozyme in the secretions. Is it possible that the presence of lysozyme effective upon a particular microbe determines its non-pathogenicity and vice versa?

The author states that a number of microbes pathogenic to animals but not to man were found to be destroyed by man's lysozyme, in particular *B. abortus* and *B. pseudotuberculosis rodentium.* Now these two organisms are identical in many respects with *B. melitensis* and *B. pestis*, both of which are, however, pathogenic to man '*and for which there is apparently no lysozyme in the human secretions*' (Reviewer's italics).

Clearly the author has opened up vast possibilities. P. F.

BIOCHEMISTRY

Raphael, T., and **Potter, F. C.** **Blood creatinin findings in five cases of corpus striatum disorder.** *J. Nerv. & Ment. Dis.*, 1922, **55**, 492.

A group of five cases was studied, including two of paralysis, two of Huntington's chorea, and one of congenital double athetosis. There was no evidence of renal disturbance. It appears from this study of five cases representing syndromes due to corpus striatum disorder that the blood creatinin values obtaining in affections of this region were very definitely below the normal minimum, affording an indication of the possibility of alteration in muscle metabolism. C. G. L. W.

Walter, F. K., u. **Genzel, A.** Untersuchungen über den Kreatinstoffwechsel bei hypertonischen Muskelzuständen, im besonderen bei Paralysis agitans. [**Creatinin metabolism in hypertonic muscular affections, especially in paralysis agitans.**] *Monatschr. f. Pschychiat. u. Neurol.*, 1922, **52**, 83.

The authors have investigated the creatin and creatinin metabolism in various forms of hypertonic condition of the muscles and have compared the results with normal individuals of the same diet. They find the variation in the relation between weight and creatinin excretion in normal subjects is greater than those that have been found in previous investigations. The creatinin excretion in women is lower per unit of body-weight than in men. They thought to reduce muscle tonus by the injection of scopolamine. The effect on the creatin elimination was not concordant. On the whole the results showed that the metabolism was unaffected by the drug.

In general, they do not find an increased creatinin elimination in hypertonic conditions. C. G. L. W.

WAGNER, R. Über Phlorhizinglykosurie. Nach Versuchen die an einem Falle besonderer Kohlenhydratstoffwechselstörung angestellt wurden. [**Phlorizin glycosuria. Experiments on a case with abnormal metabolism.**] *Ztschr. f. d. ges. exper. Med.*, 1922, **28**, 378.

Wagner has enlarged his observations on the interesting case of glandular insufficiency previously abstracted (*Medical Science*, 1922, **6**, 161) and has used the case to ascertain the seat of phlorizin glycosuria. The child received the glucoside fasting and with sugar, and the amounts of sugar in the blood and urine were followed. The results indicate that the amount of sugar excreted is independent of the amount of sugar in the blood. The amount of phlorizin had no effect on the quantity of sugar eliminated. The point of attack of phlorizin is the kidney, where it acts upon the parenchyma and stimulates it to sugar secretion. As the author points out, this explanation is difficult to reconcile with the idea of a filter which is independent of the concentration of the fluid which it is filtering.

C. G. L. W.

KRAUSS, E. Der Harnsäuregehalt des Blutes bei Erkrankungen der Niere im Vergleich zum Reststickstoff und Kreatinin. [**The relation of uric acid in the blood to rest nitrogen and creatinin in diseases of the kidney.**] *Deutsches Arch. f. klin. Med.*, 1922, **138**, 340.

The author has examined the uric acid content of the blood in a varied series of cases, in the attempt to ascertain whether the retention of this substance precedes the retention of urea and of the other substances constituting the rest nitrogen fraction. He does not find, as Folin and Denis have stated, that an increase in the concentration of uric acid in the blood is always associated with a gouty diathesis. It is often raised in leucaemia, severe toxic conditions, polycythaemia, uncompensated heart lesions, and many forms of carcinoma. In the pre-mortal rise of the rest nitrogen uric acid takes an important place.

In acute nephritis uric acid in the blood increases before the increased concentration of urea takes place, and remains high longer during convalescence, and in chronic conditions is the only indication in the blood of a pathological change in the kidney. Values higher than 10 mgm. per cent. denote an unfavourable prognosis. In the nephroses the uric acid content is normal. In the cases of benign contracted kidney there is an increased uric acid, accompanied by changes in the elimination of water, &c.

Pure hypertonia without any indication of kidney disease is accompanied by an increase in uric acid in the blood. Uric acid determination may conveniently replace rest nitrogen. Estimations for a normal value for the latter correspond to the same for uric acid. C. G. L. W.

LILJESTRAND, G., u. **STENSTRÖM, N.** Wirkung von Massage und passiven Bewegungen auf Gaswechsel und Minutenvolumen des Herzens. [**Effect of massage and passive movements on the gaseous exchange and the minute volume of the heart.**] *Skand. Arch. f. Physiol.*, 1922, **42**, 81.

The effect of various forms of massage and of passive movements on the metabolism and on the circulation was studied by careful observations in two normal persons. While the minute volume of the heart remains unaffected, respiration and gaseous metabolism show very considerable alterations. The frequency and depth of the respiratory movements is increased. The absorption of oxygen is greatly increased. In some cases the increase amounted to 45 per cent. of the resting value. The respiratory quotient rises, partly as the result of the driving off of CO_2. W. C.

Rewiger, K. Über den Einfluss kleiner Mengen Methylalkohols auf den Stickstoffstoffwechsel. [**The influence of small amounts of methyl alcohol on nitrogen metabolism.**] *Ztschr. f. d. ges. exper. Med.*, 1922, **28**, 368.

Methyl alcohol administered to partly fasting dogs induces loss of nitrogen, even when the dose is a non-toxic one. The same occurs with amyl alcohol. C. G. L. W.

Oliver and **Yamada, S. S.** **Biological reactions of arsphenamine. III. Its immediate toxicity as contrasted with its late ill effects and the rôle of agglutination in the production of the former.** *J. Pharmacol & Exper. Therap.*, 1922, **19**, 393.

It is known that the symptoms of arsphenamine (salvarsan) poisoning may be divided into those which are early, evidenced by sudden collapse and death, and late symptoms involving the skin, the kidneys, or the liver.

The authors have studied the effects of salvarsan on rabbits by administering doses which will produce the one or the other type. Microscopical examinations of the organs were made. The early toxic symptoms are connected with physical changes produced by the drug on the blood leading to multiple embolism by agglutinated red cells. The delayed symptoms are due to chemical toxicity, contingent on the chemical constitution of salvarsan rather than on any physical changes it may induce in the cells of the body. C. G. L. W.

Weiss, S., and **Thatcher, R. A.** **Studies on strychnin.** *J. Pharmacol. & Exper. Therap.*, 1922, **19**, 419.

Of clinical interest in this paper is the determination of the rate of excretion of strychnine in man. The experiments were performed upon the authors. Single doses of 0·004 mgm. were used orally and intramuscularly. In 12 hours 20 per cent. of the drug is excreted when administered in one dose. Smaller divided doses are eliminated more slowly Diuresis hastens excretion but does not increase the total amount. The liver appears to be the main protecting organ against strychnine poisoning. C. G. L. W.

Bijlsma, U. G., u. **Roessingh, M. J.** Die Dynamik des Säugetierherzens unter dem Einfluss von Stoffen der Digitalisgruppe. [**The dynamics of the mammalian heart under the influence of substances of the digitalis series.**] *Arch. f. exper. Path. u. Pharmakol.*, 1922, **94**, 235.

Using the heart-lung preparation of Starling and his co-workers, the authors have investigated the effect of strophanthin on the mammalian heart. They find (1) that if the venous inflow, being high, is kept constant, then strophanthin causes an increase in the output of the heart per minute; (2) that after strophanthin the heart can deal with a greater venous inflow than before; (3) that for a given venous inflow, when the heart is working against a given arterial resistance, the volume of the heart is smaller when it is under the influence of strophanthin. The therapeutic effect of strophanthin consists in a change in the physiological properties of the heart-muscle, so that the same mechanical effect is obtained at a shorter initial ventricular length. If external conditions remain the same, there is a diminution of the heart-volume under strophanthin, so that the extent to which the heart can dilate under greater stress is increased. J. H. B.

Riesser, O., u. **Neuschlosz, S. M.** Physiologische und kolloidchemische Untersuchungen über den Mechanismus der durch Gifte bewirkten Kontraktur quergestreifter Muskeln. V. [**Physiological and colloid chemical investigations into the mechanism of the contracture of striped muscle produced by different poisons.**] *Arch. f. exper. Path. u. Pharmakol.*, 1922, **94**, 190.

Various substances which have the physiological property of being able to affect the contraction of striated muscle, such as veratrin, strophanthin, quinine, caffeine, and nicotine, have also a remarkable effect on the viscosity of solutions of gelatin. The effect of the viscosity depends on the hydrogen-ion concentration, and on the concentration of the drug; thus with increasing concentrations of veratrin the viscosity first increases and then decreases. The authors suggest that the effect of veratrin on striped muscle receives its explanation in this phenomenon. The concentration of veratrin outside the muscle-fibres will be greater than that inside; hence near the surface there will be a lowering of the force of inhibition (entquellende Wirkung) exerted by the muscle proteins, and in the middle of the fibres there will be the opposite effect. Hence the relaxation of the muscle will be greatly delayed. Drugs such as veratrin and novocaine, which are antagonistic in their effect on striped muscle, are also antagonistic in their effect on the viscosity of gelatin. J. H. B.

de Boer, S. Über die Wirkung von Chinin bei Vorhofflimmern. Ein therapeutisches Paradoxon. [**On the effect of quinine in auricular fibrillation. A therapeutic paradox.**] *Arch. f. exper. Path. u. Pharmakol.*, 1922, **94**, 314.

The treatment of auricular fibrillation by quinine or quinidine is held to be paradoxical because the action of these drugs is to lengthen the refractory period. The author holds the view that, when the refractory period increases, the metabolic condition of the heart becomes worse. His theory enables him to give a new explanation of why only a certain percentage of cases of fibrillation are cured by quinidine. The fate of any case under this treatment depends, he argues, on predisposition. The cause of fibrillation is the poor metabolic condition of the auricles, as a result, for example, of mitral stenosis. Quinidine, in stopping the fibrillation, still leaves the auricles in the same poor condition, with the result that the fibrillation often starts again. J. H. B.

Wels, P. Untersuchungen zur Frage der inneren Desinfektion (Reagensversuche an Acridinfarbstoffen). [**Internal disinfection. *In vitro* tests with acridine dyes.**] *Ztschr. f. d. ges. exper. Med.*, 1922, **28**, 347.

The experiments were performed with substances belonging to the flavine group. The dyes were first absorbed by small pieces of the organs of animals and the toxicity of the resulting solution to staphylococci determined. The presence of serum in the solution has an inhibitory effect on the antiseptic action. The presence of large amounts of these dyes in the blood certainly increases the bactericidal action of the fluid, but smaller concentrations appear to excite growth. It is uncertain whether this effect is a pure stimulating effect, or is due to an action of the dye on the serum.

C. G. L. W.

Hirsch, P. Die Anwendung der Interferometrie auf biologische Probleme. [**The use of the interferometer in biology.**] *Die Naturwissenschaften*, 1922, **10**, 525.

The author gives a review of the interesting results which he and his co-workers have obtained by the use of the interferometer in the study of immunity reaction and the so-called 'protective ferments' of Abderhalden. This instrument is capable of detecting very minute changes in a substrate due to the action of a ferment on a protein. The tests can be made with less than 1·0 c.cm. of fluid. Hirsch finds that with his technique he can confirm the results of Abderhalden, and believes that the failures on the part of other investigators can be set down to imperfect asepsis. In this field he believes that valuable clinical results may be obtained. For example, it ought to be possible to determine whether a case of obesity is one of pituitary, thyroid, or genital origin. In cattle tuberculosis, he finds that infected animals all give a specific reaction while normal animals do not. The results were all controlled in the slaughterhouse.

Pregnancy may be detected 14 days after onset, and during the whole period of gestation it was possible to demonstrate the presence of protective ferments.

An interesting feature of Hirsch's work is the conclusion that one may use the organs of different species for specific tests.

The interferometer, as might be expected, is able to follow out quantitatively the course of a ferment reaction, such as that with pepsin, and Hirsch has elaborated a method for the quantitative estimation of this ferment by means of the interferometer. Further work has been directed to a study of immunity reaction. Reactions in which no precipitate was formed and those in which flocking occurred were studied. They find that the precipitate is certainly of a protein nature and does not consist of the antigen. It is probably the globulin fraction of the immune serum. They view the mechanism as largely chemical, in which the specific action takes place in Emil Fischer's sense of 'lock and key'. The antigen is the 'lock', the precipitin is the 'key'. The later action in which actual flocking occurs is colloidal.

C. G. L. W.

Laidlaw, P. P., and Payne, W. W. A method for the estimation of small quantities of calcium. *Biochem. J.*, 1922, **16**, 494.

Calcium is separated from the blood as oxalate and converted into calcium alizarinate. From the latter the alizarin is set free and estimated as the ammonium salt colorimetrically. An accuracy of 2·0 per cent. is obtained, which is higher than that given by other methods.

C. G. L. W.

RADIOLOGY

Radiotechnique

Clark, L. H., and **Watters, B. D.** **Comparisons between the therapeutic, photographic, and ionization effects of ultra-violet and of beta radiations.** *J. Rönt. Soc.*, 1922, **28**, 119.

The authors have made some interesting comparisons between the effects of ultra-violet radiation from a mercury lamp and the beta rays from radium upon the skin. Small portions of the arm were exposed for various lengths of time to the former radiation and the effects were compared with those obtained by other authors in the case of beta rays.

Perhaps the most characteristic point of difference in the general reaction of the skin to moderate doses of these two kinds of radiation is in the latent period, i.e. the time interval between the exposure and subsequent reaction. In the case of ultra-violet rays this is often a matter of a few minutes, whereas several days elapse before similar symptoms appear under beta ray exposures. As the authors point out, a fact of this sort must be taken into consideration in any theory which may be put forward explanatory of the processes operating.

The authors then deal in a detailed manner with experiments directed towards finding the most suitable means of measuring the intensity of sources of ultra-violet radiation for general medical purposes. Three methods were tried: (1) The energy expended in the lamp; this was tested by running the lamp under conditions so that the energy consumed varied from $9{\cdot}2$–$94{\cdot}6 \times 10^3$ Joules, and the variations in the latent period were observed. (2) Photographic comparisons were made of the intensity of different portions of the ultra-violet spectrum by the use of the following filters: aesculin, nickel glass, and phenol solutions. With filters of aesculin and nickel glass, exposures greater than those calculated to give a certain type of reaction in each case were without effect upon the skin, but in the case of phenol solution the actual exposure necessary was only about one-third of that which the photographic exposure would have indicated. This was due to the fact that the radiation transmitted by this filter was much more active upon the skin than it was upon the photographic film. Such a finding naturally sets a limit to the value of photographic methods for the purpose in question. (3) Ionization measurements were made by means of the photo-electric action of ultra-violet rays upon a zinc plate. Here a correspondence was found between the intensity of the ionization and the energy consumed in the circuit; but owing to the phenomenon of photo-electric fatigue the method cannot be put into general use. Reviewing the three methods, the authors come to the conclusion that at the present stage the energy consumed in the lamp is the most reliable of the three methods. It does not, however, overcome one difficulty which is met with in practice, namely, the opacity of the quartz-container, which is a frequent sequel to prolonged use. S. R.

Cluzet et **Kofman.** Étude ultra-microscopique de l'action des rayons X sur les colloïdes métalliques. [**Ultra-microscopic study of the effects produced on metallic colloids by X-rays.**] *J. de radiol. et d'électrol.*, 1922, **6**, 233.

It is well known that ultra-violet rays produce flocculation in pseudo-solutions of colloidal metals. Until now the action of X-rays upon metals in this state has occasioned some controversy. Cluzet and Kofman have made an exhaustive study of the subject. They submitted colloidal solutions of various metals to the action of the rays (5–7 B) both directly and modified by the presence, in the liquid itself, of secondary radiators. These secondary radiators, when made of light metals, as, for instance, aluminium, produce easily diffused rays. When made of lead or tungsten they produce the characteristic rays of the *M series.* All seem to produce beta rays.

The radiation was produced by means of a Coolidge tube with an equivalent spark-length of 7–14 cm., and carrying a current of 1·5 milliampères. The radiations lasted from 30 to 40 minutes. The control contained the same colloidal solutions and the same secondary radiators, but were not irradiated.

The authors deduce, from these experiments, that colloidal gold is the metal in which flocculation most readily occurs. It can be produced by direct radiation and better still with the aid of aluminium and copper radiators. Radiators made of lead or tungsten produce no effect at all. Analogous, but less distinct, modifications occur in pseudo-solutions of the following colloidal metals: platinum, palladium, mercury, and rhodium. The electric sign (negative or positive) of the colloids is not affected by radiation.

The new facts contained in this work deserve careful study. The varying effects produced by diffusing radiators, and those with specially characterized rays, should be carefully observed.

These papers are probably the forerunners of a series of articles on this subject which promise to be of great interest. M. B. D.

Erskine, A. W. Irradiation homogène du thorax. [**Homogeneous irradiation of the thorax.**] *J. Radiol., Nebraska,* 1922, **3**, 5. (*J. de radiol. et d'électrol.,* 1922, **6**, 193.)

In order effectively to treat cancer of the breast without fear of metastases in mediastinum and lung (a frequent cause of death in patients), the author recommends the administration, both to the mediastinal glands and to the whole lung, of approximately the same dose as to the subcutaneous growth. He suggests that in this way the neoplastic process may be totally arrested.

This is, then, the problem: to combine (for the purpose of obtaining an homogeneous irradiation) the anticathode-skin distance, the number and dimensions of the portals of entry, the voltage, and the filtration. The average depth of the deep region to be irradiated (measured in 100 women) is 4 cm. A combined study of the portals of entry and the anticathode-skin distance is necessary. If irradiation *via* several small portals of entry permits of the administering of a depth dose, inconveniences may arise, caused both by the conical grouping of the rays and the possibility of overlooking small surfaces. The author shares the views of Friedrich and Kroenig, i. e. that an increased anticathode-skin distance and an increase in the surface to be irradiated are advisable. He recommends a distance of 16 cm. and four portals of entry (each of 10 cm. diameter) for the side of the chest in question (antero-posterior, lateral, vertical), and two for the opposite side (vertical, lateral). It remains to discover the voltage-filter combination in order that $\frac{1}{4}$ of the depth unit corresponds to the portal of entry to each skin unit: the four portals of entry thus giving one whole depth unit.

The author has pursued these inquiries by means of a phantom and an ionization chamber, and has arrived at this conclusion: At least 100 kv. with a filter of 10 mm. Al or ½ mm. Cu, and he sums up as follows:

For purposes of obtaining almost homogeneous irradiation of the thorax: *four portals of entry with* 16 *cm. anticathode-skin distance,* 100 *kv. minimum, filter of* 10 *mm. Al or* ½ *mm. Cu.* M. B. D.

Radiodiagnosis

Haret. Présentation de gélatines bismuthées pour examen radioscopique de l'estomac. [**Administration of bismuthized capsules for the purpose of facilitating radioscopic examinations of the stomach.**] *Bull. Soc. d. radiol. méd. de France,* 1922, Jan., 28–30. (*J. de radiol. et d'électrol.*, 1922, **6**, 191.)

Having suffered many inconveniences by the use of a mixture (lycopodium and carbonate of bismuth) during stomach examinations (residual fluid, &c.), Haret has sought for and found a more practical and satisfactory method. He uses a gelatin composed of two oblong capsules, which telescope into each other, and inside it he places, roughly, 60 cgm. of bismuth. Owing to the presence of a small quantity of air, these gelatins float, and they follow accurately the movement of any fluid which they may encounter. They have also an additional advantage, i. e. disaggregation takes place within three minutes after contact with the gastric fluid. M. B. D.

Boigey. Le cœur pendant l'exercice physique. Examen radioscopique. [**Radioscopical examination of the heart during physical exercise.**] *Presse méd.*, 1921, Aug., 654. (*J. de radiol. et d'électrol.*, 1922, **6**, 141.)

The subjects examined by the author were young, healthy, and accustomed to physical exercise. The types were therefore not altogether normal, since the exercise always leads to a certain hypertonicity of the cardiac muscle. Moderate exercise does not lead to a great modification of the cardiac area, which has a tendency to diminish rather than enlarge. This is due to the hypertonicity of the heart, which, being slightly hypertrophied, acts with power. When the exercise is strenuous and prolonged beyond a certain limit a second phase comes on, one of hypotonicity, during which the overworked heart becomes dilated little by little and gives way. It is advisable to note this effect of too strenuous exercise so as to avoid reaching the phase of cardiac hypotonicity, especially in young subjects. The author notes having observed no difference in the cardiac area whether the subject be standing up or lying down. S. E. L.-B.

Holland, C. T. On rarer ossifications seen during X-ray examinations. *J. Anat.*, 1921, **55**, 235. (*J. de radiol. et d'électrol.*, 1922, **6**, 91.)

The article refers to rare ossifications in the foot more frequently than in the hand, which are important from a medico-legal point of view. In the foot there are ten or eleven small accessory bones (Quain's *Anatomy*, 1915), some of which are occasionally visible under X-rays. (1) The most frequent is the 'external tibial bone' at the postero-external part of the tuberosity of the scaphoid: it may be met with in children but is generally found in adults; it is not a sesamoid and is never in the tendon of the tibialis posticus. It may be mistaken for a fracture. (2) The 'os trigonum', important to recognize in fractures in the region of the instep. (3) 'Pirie's bone'

(1919), between the postero-superior part of the scaphoid and the anterior part of the astragalus. (4) 'Os Vesalianum' (1725). This was described by Vesalius as 'a small bone, opposite to the outer side of the joint, and placed proximally to the little toe, and probably articulating with the cuboid'. The author is of opinion that what Vesalius described is the sesamoid of the peroneus longus, and that the bone which is now often spoken of as the 'bone of Vesalius' is in reality an epiphysis at the base of the fifth metatarsal, which usually joins on before adult life, but in one form—a very rare one—may remain separate in the adult. (5) Köhler's disease of the scaphoid, very rare, characterized by an arrest of ossification and an abnormal opacity of the scaphoid. (6) In conclusion the author cites as the most rare the existence of a double point of ossification of the patella with more or less complete separation of the bony fragments. The author lays stress on the necessity of the examination of both limbs as the anomalies are generally bilateral, on the integrity of the bony contours in the cases, and on inquiry as to previous history (trauma, &c.). S. E. L.-B.

SOURDAT, P. L'épicondylite des joueurs de tennis. [**Tennis elbow.**] *L'actualité médicale picarde*, 1921, June, 13. (*J. de radiol. et d'électrol.*, 1922, **6**, 42.)

This affection is characterized by a very sharp pain at the level of the epicondyle during strenuous sport. The acuteness of the pain may lead to an almost complete uselessness. Rest relieves the pain, but if the player does not stop his favourite sport at once the affection may last indefinitely. Radiography shows nothing in recent cases, but in long-standing cases it shows slight bony proliferations around the epicondyle and small bony spicules at the same level. Treatment consists in prolonged rest; it alone eases the pain. S. E. L.-B.

CORONÉ. Valeur séméiologique d'une obscurité relative légère du sommet gauche à la radioscopie. [**The semeiological value of a slight relative opacity of the left apex in radioscopy.**] *Sciences méd.*, 1921, October, 40. (*J. de radiol. et d'électrol.*, 1922, **6**, 148.)

In 2,333 radioscopical examinations of the lungs, carried out by himself, the author has been struck by the frequency of a relative opacity of the left apex. He believes that when a patient suspected of tuberculosis is examined, less importance should be attached to a slight opacity if it occurs on the left side than if it occurs on the right. S. E. L.-B.

GRAF, H. Mammillenschatten im Röntgenbilde. [B.] [**Nipple shadows in the X-ray picture.**] *Beitr. z. Klin. d. Tuberk.*, 1922, **51**, 12.

The gist of Graf's paper, which includes records of eight cases, some of which are illustrated by skiagrams, is that in thin, parous women the nipples may cast shadows which are apt to be confused with those of tuberculous foci, lymphatic glands, and cross-sections of bronchi in cases of bronchiectasis. Such a mistake may be serious if, in the selection of cases suitable for artificial pneumothorax treatment, this shadow is taken as a sign of tuberculous disease in the healthier lung. According to Graf, these shadows are circular or oval, about 1 cm. in diameter, symmetrical, and demonstrable at the level of the fifth ribs in front or the fifth intercostal spaces. He also discusses the identification of these shadows with their cause by means of metal rings secured to the nipples. C. L.

MEDICAL SCIENCE

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NOTICE.

In the references the letter [B] after the title signifies that the original memoir contains a good bibliography of the subject dealt with.

REVIEWS

GONORRHOEA

Symptomatology. McDowell reports a case of *keratosis blenorrhagica* in which the lesions were scattered over the lower limbs and back as well as affecting the soles. The patient also suffered from arthritis of the hip and ankle and gonorrhoeal arthritis. In a case reported by Gager the affection is said to have commenced as a vesico-pustular eruption, the lesions of which afterwards became cornified with much thickening of the epidermis. Gram-negative diplococci (gonococci) were found in the contents of the vesicles, and were also present in the urethral secretion. In this case the eruption was bilateral and distributed irregularly over the greater part of the body, including the glans penis and prepuce. There was concomitant arthritis of the knees and ankles. Jeanselme and Blamoutier describe a case in which the glans penis only was affected, in the form of two horny lesions, one on each side of the glans. After these were removed gonococci were found both microscopically and by culture in the exudation from the base of the lesions. There was a history of gonorrhoea five years previously and a persistent 'morning drop', but no other signs of gonococcal septicaemia.

Liebe reports a case of *bullous exfoliative dermatitis* in an infant, occurring four days after birth and affecting chiefly the hands, face, and scalp. Intracellular gonococci were found in the fluid from the bullae, and also in the mother's urethra. The eruption was cured by the application of strong silver nitrate solution.

Simmons reports a case of *gonococcal pyelitis* which was discovered during an operation for ruptured kidney. A pure culture of gonococci was obtained from the pus from the kidney pelvis. He considers that haematogenous infection is more probable than direct ascending infection either by mucous membrane or lymphatics.

Norris and Mickelberg, in examination of 74 cases of *vulvo-vaginitis* in children, found that the cervix was affected in nearly all, and Bartholin's ducts and the urethra in many of the cases. Complications were rare, including only one case of arthritis: infection of the tubes and ovaries was not observed in any case. The authors attribute the absence of tubal complications to the absence of menstruation and pregnancy—the periods during which upward extension of the disease usually takes place in the adult. Recurrences they found to be generally due to an undetected focus, usually in the cervix, but sometimes to reinfection. They remark that the disease nearly always undergoes spontaneous cure before puberty.

Luker reports a case of *gonorrhoeal cervicitis* in a young woman which was followed in five months by carcinoma. He suggests that the chronic discharge together with repeated applications of silver nitrate acted as irritating causes.

Bizard and Blum conclude that the gonococcus is nearly always the cause of *Bartholinitis*, and that staphylococci and streptococci, which are found in some cases, are due to secondary infection. Cases apparently banal may relapse, and gonococci will then be found in the pus. Lippert, on the other hand, reports a case of non-gonococcal Bartholinitis, occurring in an alleged virgin aged 17, in which *B. coli* were found but no gonococci.

Clodi and Schopper found *gonococci in the secretion of the preputium clitoridis* in 74 per cent. of cases of gonorrhoea in women, and point out the necessity of thorough disinfection of the folds of this appendage, infection of which is a constant source of reinfection and contagion.

O'Connor, in a critical review of the reported cases of *gonorrhoeal affection of the nervous system*, sums up as follows: In rare cases the gonococcus has been found in the central nervous system, and the lesions caused thereby are probably of the nature of metastases. Similar effects may, however, be produced by the toxin, and there is often a mixed infection. The toxaemia of gonorrhoea may produce psychopathic effects, the chief of which are neurasthenia, hypochondriasis, and melancholia. There is also some evidence of a gonorrhoeal hysteria, and of toxic delirium which may rarely develop into acute mania. Gonorrhoea may also act as an exciting cause in latent mental disorder. The existence of a gonorrhoeal cerebrospinal meningitis is well established both clinically and pathologically: also of meningo-myelitis. A gonorrhoeal polyneuritis, however, is not so clearly established. Various neuralgias may occur; Delamere describes lumbo-abdominal, crural, tibial, median, radial, trifacial, and sciatic, the latter being by far the most common. Gonorrhoeal sciatica, first established by Fournier, may be unilateral or bilateral, accompanied or not by arthritis, and may not appear till the urethritis is apparently cured. O'Connor concludes that the complications of gonorrhoea are of complex aetiology and cannot be attributed to the gonococcus alone.

Lindenfeld reports a case of *gonococcal meningitis* in a man aged 53, who died from septicaemia. The autopsy showed acute purulent cerebrospinal meningitis and also an abscess in the left seminal vesicle. Pus from these two sources showed Gram-negative intracellular diplococci. Cultures failed. The diagnosis lay between meningococci and gonococci. Examination of the prostate, testicle, and seminal vesicles showed old inflammatory changes suggesting gonorrhoea. Lindenfeld therefore concludes that the gonococcus was the origin of the meningitis, and that the case was not one of metastatic meningococcal lesions. The failure of culture he attributes to the high temperature before death. He refers to a similar case published by Prochaska, in which there was also pus in the seminal vesicle, and in which the gonococcus was cultured from the blood, meninges, and seminal vesicle.

Diagnosis. Montpellier and Lacroix have investigated the practical value of the *gonococcal reaction*. The antigen used was the antigonococcal vaccine of the Institut Pasteur, and their conclusions are as follows: (1) The results were always negative in persons free from gonorrhoea; (2) the highest percentage of positive reactions was obtained in simple acute gonorrhoea; (3) the results were often negative in acute gonorrhoea with complications, which they explain by absence of gonococcal reagin in the serum in gonococcal septicaemia; (4) the results were negative in chronic gonorrhoea without complications; (5) in chronic gonorrhoea with complications, old or recent, the results were negative with heated serum, positive with unheated serum ; (6) the presence of syphilitic antibodies in the serum had no influence on the reaction.

Osmond reports the result of 1,000 *complement-fixation* tests in gonorrhoea, comprising 300 males and 700 females. He found 85 per cent. positive results in cases of active gonorrhoea, and only 3 false positives in the whole series. He concludes that the diagnostic value of complement fixation in gonorrhoea is as valuable as the Wassermann test in syphilis, that it gives a positive result earlier in the disease, but persists for some time after cure. The technique used was that of Thomson (*Medical Research Committee Special Report Series*, No. 19).

Osmond's results are criticized by Priestley, who holds that the reaction does not become positive so early, and that cases in which this apparently occurs are not new infections but relapses. Nor does he find that the test remains positive long after cure. Priestley regards the test as of very limited value as regards prognosis, as he found it to vary from positive to negative and vice versa without agreeing with the clinical signs. A positive reaction is valuable as indicating a focus of disease which is perhaps not clinically obvious, but repeated negative reactions are no criterion of cure.

Kelley has investigated Robinson and Meader's *precipitin test for gonorrhoea* (see *Medical Science* 1921, **4**, 213) and finds that the reaction is not specific. Extracts from infections due to other organisms than gonococci gave reactions both with antigonococcal and normal serums. Attempts to remove the non-specific factor, by dilution of serum and extract, &c., were unsuccessful.

Treatment. Rivaz and Hitch have analysed the results of *orthodox treatment of gonorrhoea* in 1,000 consecutive cases in the Navy. The treatment was divided into three categories: (1) irrigation only, (2) irrigation plus vaccines, (3) irrigation plus injection of colloidal metals. The statistical tables appear to show that there is not much advantage in the addition of vaccines or colloidal metals to the scheme of treatment; but, as the latter methods were reserved for cases which did not improve under irrigation only, the statistics are misleading. Comparing the statistics of cases treated by vaccines and colloidal metals, the results are approximately the same; but, as the worst cases were put on vaccines, the authors conclude in favour of the latter, and consider that they cut short the disease and reduce the liability to complications. The incidence of arthritis was reduced from 3·75 per cent. in cases treated by irrigation only to 1·54 in cases treated by vaccines. The vaccine used was prepared from cultures made from early acute cases on trypsin-legumin-agar with 10 per cent. human blood. The method of treatment by colloidal metals was that of McDonagh, viz. 2 subcutaneous injections of colloidal palladium, 0·5 c.cm., at 48-hour intervals, followed by 4 intramuscular injections of colloidal manganese, 0·5 up to 2 c.cm. The routine treatment for acute cases consisted in anterior irrigations for the first few days, then total irrigations, the drug preferred being permanganate of potassium. In chronic cases, the methods included the suction apparatus, prostatic and vesicular massage followed by an atropine suppository of $\frac{1}{75}$ grain, Kollman's dilators, &c. The authors remark that urethroscopic examination often failed to localize the lesions, even when gonococci were present. Gonorrhoeal rheumatism was treated by radiant heat, diathermy, massage of the muscles above and below the affected joints, aspiration of the joint if much distended, and vaccines. The authors warn against over-treatment in chronic gonorrhoea, and remark that cases often recover when treatment is left off. The statistics show that out of 672 fresh cases 8·18 per cent. developed posterior urethritis, 7·14 per cent. epididymitis, 2·67 per cent. arthritis, 2·97 per cent. submucous infiltration, and 2·5 per cent. periurethral follicles. In 168 chronic cases no lesions were discovered in 43; posterior urethritis was present in 31, epididymitis in 35, arthritis in 19, periurethral follicles in 4, submucous infiltration in 18, stricture in 10. The invalidings from the service on account of gonorrhoea amounted to 1·7 per cent. The *tests for cure* adopted were stringent. After absence of urethral discharge for 5 days, clear urine in two glasses, negative prostatic and vesicular examination, clinically and bacteriologically, and negative urethroscopic examination, all treatment was suspended and the patient ordered to take hard exercise and stimulants. A provocative injection of 250 million gonococcus vaccine was given, and in 6 days a smear obtained by the suction apparatus was examined, together with sediment from the morning urine. If all results were negative, the programme was repeated in a month. However, even these tests were not conclusive, for relapses were found to occur after all tests were negative at both examinations. The authors consider the complement-fixation test of little value.

Fraser gives his views on the *treatment of acute gonorrhoea* in the male. For irrigation he prefers potassium permanganate 1 in 12,000 to 1 in 8,000, with the addition of 0·5 per cent. sodium carbonate; zinc permanganate, 1 in 10,000 to 1 in 6,000; oxycyanide of mercury, 1 in 8,000 to 1 in 4,000, when secondary organisms are present; silver nitrate, 1 in 20,000 to 1 in 10,000 in chronic urethritis. As regards the mode of action, he considers the chief effect to be due to flushing and possibly chemotoxic action, the drugs being too dilute to have any germicidal action. Acriflavine, although it soon reduces a purulent discharge, leaves a muco-purulent one which is difficult to cure, and seems to damage the urethral mucous membrane. The organic silver preparations, protargol, argyrol, &c., he regards as useful for abortive treatment, but of little use when the disease is established, as they are mostly colloidal emulsions with little penetrative power, and are all astringent and precipitate proteins, thereby interfering with drainage. One of the most useful preparations consists of 1 per cent. albargin in gelatin, tragacanth, and glycerine. Picric acid is irritative and inferior to zinc permanganate. Perchloride and biniodide of mercury are also irritative, even in dilutions of 1 in 20,000. Zinc, copper, and alum are inferior to silver nitrate. Chemotherapy is favoured by Fraser, but in its present status, as an adjunct only to local treatment. Although McDonagh's theory of oxidation and reduction is a matter of controversy, there is much in favour of his treatment by colloidal metals and intramine. A good plan is to commence with 1 c.cm. of colloidal palladium in the early stage of gonorrhoea and follow with 0·5 c.cm. colloidal manganese at intervals of four days till the discharge ceases. Trimine, or colloidal ferro-manganese and zinc, may replace manganese. In chronic cases intramine is indicated in doses of 2·5 to 5 c.cm. Trimine and intramine are more effective in complications, such as arthritis, prostatitis, vesiculitis, and gonococcal dermatosis. Fraser makes no mention of the recent arsenical treatment of gonorrhoea. As regards vaccines, he thinks their value in acute gonorrhoea has been proved. Good results have been obtained with the English 'staphgon', a stock vaccine containing 50 million gonococci and 150 million staphylococci, and with 'dmegon', a similar French preparation made by Nicolle and Blaziot. According to Fraser, the acute stage is shortened and there is less liability to relapse after a course of one of the above. He does not consider sensitized vaccines satisfactory, but regards detoxicated vaccines as the best of all. With these, toxic reactions are avoided, larger doses are permissible, and the negative phase is eliminated. They must, however, be made of the proper strains; but, as the gonococcus, especially since the War, has become more 'cosmopolitan', detoxicated gonococcal vaccines are more successful than detoxicated vaccines for other infections, in which there is greater local variation in the strains.

Cunningham and Cook discuss the *operative treatment of acute gonorrhoeal epididymitis.* Comparative results of expectant and operative treatment in severe cases are, they maintain, in favour of the latter procedure. Sterility is not greater after bilateral epididymotomy, but probably less. The operation causes rapid relief of pain and fall of temperature, and the patient can resume his work much sooner than with expectant treatment. Examination of the tissues shows that small abscesses are frequent, and that there is a rapid destructive process in the tubules and intertubular tissue. Hence the indication for early surgical drainage in cases which are clinically severe.

Paul reports the results of treatment of 100 cases of *chronic urethritis and its complications.* The time since the last acute infection varied from 2½ months to 20 years; the duration of treatment from 5 to 48 weeks. In 66 cases there was a matutinal urethral discharge; in the remainder this was absent, the symptoms including filaments in the urine, various disorders of urination, urethral discharge after stool, signs of old epididymitis, arthritis, &c. In the 66 cases with urethral discharge gonococci were found in the discharge in 4 instances only before treatment, but in 18 after treatment was in progress, and in 44 cases in the prostatic and seminal secretion after treatment. In 22 cases the original diagnosis had been non-specific urethritis, often after repeated microscopic examination; 9 of these showed gonococci after treatment was commenced. This is said to disprove Keyes's statement that gonococci do not survive for more than three years in the male urethra; but no mention is made as to culture. Complications included 24 cases of old epididymitis, 8 strictures, 4 requiring urethrotomy, 12 instances of sexual neurasthenia, which generally disappeared during treatment. Syphilis was found in 6 cases only, and only 2 gave a positive Wassermann reaction. Treatment was essentially local. No drugs were given by hypodermic or intravenous injection. Vaccines were used in about 60 cases, but the benefit obtained thereby was doubtful except in those cases with gonococci in the secretions, when pure gonococcus vaccine in maximum dosage appeared to hasten the disappearance of the gonococci. Bougies of metal and elastic web were used for dilatation of the urethra, always followed by antiseptic irrigation. Kollman's dilators were tried in a few cases, but afterwards discarded as being too injurious. For irrigation, instillation, &c., the following drugs were used: oxycyanide of mercury, mercurochrome, potassium permanganate, zinc sulphate, chlorozone, iodine, silver nitrate, and the organic silver compounds, such as argyrol, nargol, silvol, protargol, and nucleinate of silver. Of all those, silver nitrate appeared to be the best. Massage of the prostate and seminal vesicles was done in every case in which those organs were affected, and was continued till the secretion showed only one or two pus cells in the microscope field. This was preferred to vas puncture and other operations on the seminal vesicles. In 16 cases with rheumatic symptoms, however, operative measures were considered necessary; injections of the vas deferens in 2, epididymotomy in 2; perineal section for drainage of the prostate and seminal vesicles in 4, paracentesis of the prostate and injections of 30 c.cm. of Cano's phenol serum in 2 cases. In most of these cases the rheumatic and urethral symptoms were cured or improved. Meatotomy was performed in 27 cases to facilitate drainage and local treatment. The author concludes by drawing attention to the danger of passing a patient with a chronic urethral affection as non-infectious, the good results of appropriate treatment in deep-seated infections of the urethral mucosa, the persistence of the gonococcus in the male urethra and its adnexa, the occasional long incubation period and absence of symptoms in gonorrhoeal urethritis.

Lévy-Weissmann urges that more attention should be paid to the *chemiotherapy of gonorrhoea,* pending possible improvements in vaccine therapy in the future. Vaccines, he remarks, have no constant action in shortening the duration of urethritis or preventing complications, although they are often effective against such complications when they have developed. Serotherapy he considers hardly more efficacious, and points out that some of the most successful results have been obtained with non-specific serums such as antimeningococcic, antidiphtheritic, and simple horse serum. As regards chemiotherapy, mercury, iodine, and arsenic have given promise. Thus, Stern and Ridler reported good effects from intravenous injections of 20 c.cm. of a 16 per cent. solution of sodium iodide in gonorrhoeal arthritis, epididymitis, and prostatitis; and Pareira from mercurial injections in acute and chronic gonorrhoea. More recently, Lévy-Bing and Janet have obtained good results with arsenic, in the form of salvarsan or neosalvarsan, and Lévy-Bing and Duroeux with sulfarsenol in gonorrhoeal complications. Lévy-Weissmann was led to try chemiotherapy in gonorrhoea by the chance observation that a patient who was being treated for primary syphilis with injections of mercuric cyanide and sulfarsenol was cured of a coincident gonorrhoeal urethritis. He then successfully treated 5 cases—2 of acute prostatitis, 2 of chronic prostatitis, and 1 of epididymitis, with *sulfarsenol.* The drug was injected intramuscularly in doses of 12 to 18 cgm. every other day, from 4 to 10 injections being given. The usual local treatment had failed in the cases of chronic prostatitis. Lévy-Weissmann thinks that the arsenical preparations reinforce the usual treatment by modifying the soil and shorten the duration of the infection.

Good results from arsenical treatment are claimed by Mouradian in *gonorrhoeal salpingo-ovaritis and orchitis,* both acute and chronic. The drugs he used were novarsenobenzol or neosalvarsan, commencing with 0·15 gm. and gradually increasing to 0·75 gm. He concludes that the drugs act directly on the gonococci, and that failure is due to the presence of secondary organisms, in which case an autovaccine should be administered in addition.

Russ gives the results of further experience with his method of treatment by *electrolysis.* This method consists in passing a perforated catheter, containing a stylet, as far as the compressor muscle, filling it with a 1 per cent. solution of sodium chloride and $\frac{1}{2}$ per cent. of monochloracetic acid, and passing a current of three-quarters to one milliampere through the stylet, which is connected with the positive electrode. The negative electrode, of metallic gauze, covered by lint wrung out in warm water, is placed on the scrotum and around the penis. The current is passed for half an hour daily for five days, afterwards every other day. An average of 12 applications is enough. Accessory treatment by vaccines and sandalwood oil is also given. According to Russ this method gives more reliable results than irrigation in acute gonorrhoea and is less liable to complications. Chronic cases are also said to be cured by this method.

Nanta considers that failure in the *vaccine treatment* of urethritis is often due either to incorrect bacteriological diagnosis or to too much uniformity in method. Gonorrhoeal urethritis which fails to improve with a stock vaccine or with small doses of an autovaccine will often yield to large doses of autovaccine, which is the best for such cases. For staphylococcal urethritis small doses of autovaccine are sufficient.

Langer describes the methods found most useful in Buschke's Clinic at the Rudolf Virchow Hospital in the treatment of *gonorrhoeal joint and tendon affections.* The general principle of treatment is conservative, surgical measures and even puncture being avoided as far as possible. For all mild and subacute cases with not much effusion, active and passive movements are commenced from the beginning. These are carried out in a hot bath, either local or general, one or two baths being given daily for a quarter or half an hour. Between the baths 25 per cent. ichthyol ointment or iodine vasogen is applied, with or without a splint according to the case. Internally, sodium salicylate, aspirin, potassium iodide, or pyramidon are given, and 3, 5, and 7 c.cm. of sterilized milk by intramuscular injection at intervals of two or three days. Sometimes intravenous injection of vaccines is performed. This treatment is found successful in the case of small joints and tendons. In severer cases with much swelling, especially of the larger joints, treatment is commenced with rest and fixation in splints, and, if there is much effusion, light compression of the joint. Considerable experience is required to decide when to leave off fixation, which, if continued too long, will lead to stiffening of the joints and atrophy of the muscles. Accessory treatment includes hot-air treatment two or three times daily for half an hour to an hour, or Bier's passive congestion, beginning with one hour and increasing to 18 or 20 hours. When acute symptoms have subsided, active and passive movements in the hot bath are commenced. The joint itself is not massaged, to avoid mobilizing latent gonococci. The same drugs are given as in the milder cases. The urethra is also treated. After-treatment includes massage and electrical treatment of the muscles above and below the joint, hot sand-baths, diathermy, and exposure to sunlight. Treatment by vaccines and proteins is regarded as insufficient alone, but useful as accessory treatment. The authors mention three cases of interest; one of peroneal neuritis, one of multiple myositis, and one of recurrent arthritis of the knee occurring 7 years after infection, which they regard as a case of latent gonorrhoea.

Collings claims good results in *gonorrhoeal arthritis* from the application of thick plaster of Paris casts. These are kept on for two weeks and reapplied for another two weeks after movement and massage. After this, radiant heat at 150° F. is applied for half an hour daily for the first four days, then for one hour at 200° F., combined with massage. In 26 cases so treated the duration of treatment varied from 18 to 81 days. The author considers this method superior to the use of vaccines, serums, drugs, or operations on the seminal vesicles.

Ross has treated 30 cases of gonorrhoeal arthritis with intravenous injections of *electrargol* (5–10 c.cm., combined with a mixed vaccine of gonococci, streptococci, staphylococci, and *B. coli,* and massage of the prostate and vesicles. He found that in arthralgia and polyarthritic cases pain and inflammation subsided, but in chronic hydrarthrosis the results were not so good.

Trossaello reports on the *milk treatment* of gonorrhoeal affections, 90 cases being treated with sterilized cow's milk and 10 with Müller's 'Aolan' (see *Medical Science* 1921, **4**, 214). The cases included venereal bubo, gonorrhoeal epididymitis, arthritis, prostatitis, and urethrocystitis. On an average four injections were given in doses of 5 to 10 c.cm. Early buboes subsided in one to three weeks, but more advanced ones required incision. The results were good in epididymitis and in one case of suppurative arthritis, but uncertain in prostatitis. Aolan was found to be inferior to milk in therapeutic effect.

Simmonds reports good results from *diathermy in chronic gonorrhoeal prostatitis.* A metal electrode was placed in the rectum (previously emptied), the other electrode, of lead foil, over the os pubis. A current of 1 to 2 ampères was passed for 15 to 20 minutes. The action is said to be both hyperaemic and bactericidal. Simmonds mentions experimental inoculation of rabbit's knee-joints with gonococci by Lacquers, who found the fluid from the joints sterile after diathermic treatment.

Weill-Hallé and Chabanier had success from *serotherapy* in two cases of gonorrhoeal polyarthritis, one of which was of 15 years' duration and had been unsuccessfully treated with vaccines. The serum used was that prepared at the Institut Pasteur and was administered, partly subcutaneously and partly intramuscularly, in daily injections of 40 c.cm., four injections being given in each case. The joints were restored to normal condition. Each case was followed by serum fever with rise of temperature, arthralgia, and a morbilliform rash. This was successfully treated by two or three intravenous injections of ½ to 1 c.cm. of 50 per cent. solution of calcium chloride.

Sacquépée also obtained a cure with antigonococcal serum in a remarkable case of gonorrhoeal septicaemia complicated by diphtheritic, streptococcal, and pneumococcal infections. The patient contracted gonorrhoea and diphtheria at about the same time; the diphtheria subsided, but a state of septicaemia supervened. The symptoms were not characteristic, consisting in erythema and subcutaneous oedema, neuralgias, and transitory articular signs. The temperature was at first continuous or remittent, afterwards intermittent. Blood cultures showed gonococci on two occasions and streptococci once. The septicaemia yielded to treatment by intravenous injection of antigonococcal serum after failure of gonococcal vaccines, and an intercurrent pneumonia subsided under treatment by intravenous and subcutaneous injections of antipneumococcal serum. Sacquépée considers that the evolution of gonococcal septicaemia was modified by diphtheritic infection, and that the streptococcal and pneumococcal infections were secondary.

Arnold compares *intravenous injections of gonococcus vaccine* with *intramuscular injections of turpentine* in gonorrhoeal prostatitis. He concludes that the latter method gives the more favourable results. The preparation used was 'terpichin', a mixture of pure turpentine with quinine, and was administered intramuscularly at intervals of 3 days in gradually increasing doses from 0·5 c.cm. up to 3 c.cm., for a course of six or seven injections. The injections are said to be comparatively painless. Local treatment was given also.

Ravichi, in 90 cases of *gonorrhoeal epididymitis,* obtained beneficial results with *intravenous injections of sodium iodide.* The drug was made up in ampoules with an isotonic base in doses of 2 gm. Injections were given every other day at first; later, every 3 or 4 days. The number of injections varied from 2 to 10. Treatment was ambulatory.

Cassel and Lilienthal report good results with the following method of *treatment of gonorrhoea in women* in an out-patient clinic. Twice or thrice weekly the urethra is injected with 3 per cent. protargol or 2 per cent. albargin solution, and the vagina plugged with ichthyol glycerine tampons (20 per cent.) after treatment of the cervical canal with Lugol's solution, 50 per cent. formaldehyde or 10 per cent. silver nitrate. As long as gonococci are present, home treatment is carried out by douches of weak formaldehyde solution, and by permanganate of potassium douches when gonococci have disappeared. Most patients were also taught to use 10 per cent. protargol bougies for the urethra. Out of 232 cases thus treated, 144, or 61 per cent., were negative after testing urethral and cervical secretions after the menstrual periods—127 within 6 months. The complications were few and not more than usually occurs with in-patient treatment.

Norris remarks that the chronicity of gonorrhoea in women and its resistance to treatment is due to the structural peculiarities of the female genital tract, which prevent antigonococcal agents reaching the more deeply situated gonococci, which constantly produce reinfection; also, to the presence of mucus, which retards the action of drugs. The three most obstinate situations are the cervix, Skene's tubules, and Bartholin's glands, all of which contain deep mucous glands. In the case of Bartholin's gland, infection of the duct can be cured by injections, but if the gland is infected it should be excised. The normal gland is usually not palpable, but the infected gland is enlarged and tender. Excision of the gland is facilitated by the injection of the duct with methylene blue. Urethritis is transient in women unless Skene's tubules are affected, when it becomes obstinate; the tubules should be destroyed by the cautery. Treatment of the cervix is difficult owing to the presence of crypts and folds containing tenacious mucus. The lower part of the cervix should be dilated, care being taken not to dilate the internal os, and methylene blue, mercurochrome, or Dakin's solution (1 to 5 per cent. in olive oil) applied after removal of mucus. Trachelectomy, or excision of the infected mucous membrane, should only be performed in very obstinate cases.

For *gonococcal vulvo-vaginitis in children* Norris and Mickelberg recommend vaginal injections of one part of Dakin's solution to 99 parts of olive oil night and morning, the labia being held together for two minutes after the injection; and the external genitalia cleansed with the same mixture. The cervical canal was treated with a 1 or 2 per cent. solution of mercurochrome. In 63 cases treated in this way there were only 8 recurrences. The duration of the disease varied from 3 days to 3 years, the duration of treatment from 2 to 26 weeks. In cases resistant to this method the vagina was swabbed out with permanganate of potassium solution (1 in 10,000) through a wire urethral speculum, and then ballooned with hot air for 20 to 30 minutes. A dentist's hot-air bulb can be used for this purpose. The ballooning obliterates the vaginal folds; the desiccation caused by the hot air inhibits the vitality of the gonococci, and the exposure to air is said to favour the development of squamous epithelium, which is resistant to gonococci. This treatment is performed thrice weekly. In addition, the

Dakin oil and mercurochrome are applied as above twice daily. In 11 cases thus treated (average 8 weeks) there were 2 recurrences.

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C. F. M.

DYSENTERY

I. BACILLARY DYSENTERY

Epidemiology. According to Bernstein, Kling, and Rosenblatt, immediately before the War, Vienna, like all large cities in Europe, was practically free from dysentery, only 70 cases being notified in 1913. In 1914, 1,279 cases were notified in soldiers, and in 1915 the number of notifications rose to 2,075, but rapidly decreased as the war progressed and field hospitals were built. From 1916 onwards an average of 300 notifications was made annually from the military hospitals to the city sanitary authorities. During the first three years of the war dysentery did not spread much among the civilian population. In 1914 there were about 300 notifications, in 1915 only 150, and in 1916, 200. It was not until the summer of 1917 that the first epidemic of dysentery broke out among the civilian population of Vienna, when 2,229 cases were notified. There were subsequent epidemics each year, the notifications increasing to 2,316 in 1918, and 3,355 in 1919. In 1920 isolated cases occurred during the early part of the year, there being about 20 cases a month on the average, but the period of 14 weeks between July 1 and October 14 was characterized by an epidemic wave in which 1,439 cases occurred, of which 166 or 11·5 per cent. died within this period and 14 later—a total mortality of 180 cases or 12·4 per cent. The number of cases between 1 and 40 years of age was 901 or 64·8 per cent., with a mortality of 4 per cent., and between 40 and 80, 538 or 35·2 per cent., with a mortality of 24 per cent., thus showing the characteristic malignancy of dysentery in the second half of life. The writers point out that the epidemic occurrence of dysentery in Vienna since 1917, of which the recent epidemics are merely a manifestation, is the result of poverty and can only be prevented by improvement in the food, housing accommodation, and personal cleanliness.

Piltz illustrates the recent increase in the incidence of dysentery in Germany by stating that during 14 months, in the years 1911 and 1912, 15 autopsies with definite evidence of bacillary dysentery occurred among a hospital population of 774 infants, or in 1·9 per cent., whereas, during the same number of months in 1920 and 1921 post-mortem evidence of dysentery was found in 26 out of 821 infants, or in 3·2 per cent. Only those cases were taken into consideration in which the presence of dysentery was proved by the anatomical lesions. According to Piltz, bacillary dysentery is much more frequent in infants and young children than is generally supposed, and is responsible to a much greater degree than has hitherto been credited for the summer mortality of infants. He regards the bacteriological or serological proof of dysentery as much less important than the clinical symptoms and anatomical findings, although even these may be inconclusive in doubted cases of dysentery.

Violle states that numerous cases of Shiga bacillus dysentery occurred during the autumn of 1921 in the Paris suburbs, especially in the region of Maisons-Alfort and Alfortville. Children and old men were chiefly affected, and several fatalities occurred. The outbreak appears to have been due to the practice, common in the Paris suburbs, of using the contents of the latrines for manuring the gardens.

Manson and Mitchell give a brief description of a small outbreak of dysentery which occurred in Warrington in September and October 1920, the organism isolated being closely related to the Y-type. No source of infection could be traced, such as a discharged soldier or other person from an infected area. Children were principally affected.

Symptoms. Kundratitz reports two examples of a hitherto undescribed complication of bacillary dysentery in the form of *ulcerative stomatitis* followed by necrosis of the jaw in children aged 9 and 5, in a children's hospital at Vienna. Numerous cocci and other organisms in which the fusiform bacillus predominated were found in both cases.

Tscherning records a case of *chronic cholecystitis* which occurred 3 years after an attack of bacillary dysentery. As no improvement took place under medical treatment the gall-bladder was removed and submitted to bacteriological examination, which showed the presence of dysentery bacilli of the Y-type. Disease of the gall-bladder in the acute stages of dysentery has been described by Strauss, Schittenhelm, and others, but Tscherning has not been able to find any case on record in which dysentery bacilli were present in the gall-bladder so long after the onset of the disease.

According to Leusden, of Amsterdam, who records two examples, cases of *ulcerative colitis* may occur in which the only sign of a previous attack of bacillary dysentery is the agglutinative power of the blood. In such cases the symptoms are not caused by dysentery bacilli but by *B. coli*, so that ulcerative colitis must be regarded as a sequel of bacillary dysentery caused by the penetration of *B. coli* into intestinal mucous membrane which has lost its epithelium. When a strain of *B. coli* has been found treatment with an autovaccine produces an excellent result.

Kling, of Vienna, states that there are no examples on record of the transformation of acute dysentery into a severe form of colitis. He therefore reports 11 cases with 1 death, in which the direct transformation from the acute stage of typical dysentery into severe colitis could be followed by means of a series of rectoscopic examinations. All the cases occurred during the epidemic of bacillary dysentery at Vienna in the summer of 1920 and the following months, during which time 1,439 cases were admitted to hospital. In 102 or 7·5 per cent. the course of the disease was prolonged in consequence of sequelae, such as mild colitis, dyspepsia, arthritis, &c. Only 0·4 per cent. of all the cases of acute dysentery and 9 per cent. of the protracted cases developed severe colitis. Of the 11 cases 9 occurred in women and only 2 in men, showing that the female sex has a much greater disposition than the male sex for the transformation of dysentery into severe colitis. The ages of the patients ranged from 18 to 60. The following causes could be assigned for the transformation of acute dysentery into chronic colitis: (1) Lack of treatment and nursing during the acute stage; (2) an inferior constitution, shown by asthenia, chlorosis, and congenital malformations; (3) concurrent diseases.

Labbé and Bith report a fatal case of *acute hepatic insufficiency* and acidosis complicating bacillary dysentery in a woman aged 51. The diagnosis was confirmed by the autopsy which showed acute fatty degeneration and acute hepatitis of an organ which had probably been previously affected by a slight degree of periportal cirrhosis.

In a paper on *chronic dysenteric peritonitis*, Megaw, director of the School of Tropical Medicine, Calcutta, states that most of the cases of ascites which occur in the United Provinces follow on diarrhoea or dysentery, which are most probably caused by Flexner's bacillus or some closely related organism. The ascites is due to a fibrosis of the peritoneum following peritonitis, which is probably caused by the passage of an irritant toxin of bacillary origin through the wall of the large intestine. The fibrosis of the peritoneum may give rise to an excessive outflowing of fluid into the peritoneal cavity or reabsorption of fluid may be diminished. The condition is much more likely to occur in cases of dysentery treated by opiates, or not treated at all, than in those treated by salines or other aperients, in which stasis and accumulation of toxins are not apt to develop. The usual course of the disease is steadily downwards, death being due to asthenia or some intercurrent disease. The average duration of the disease is probably less than six months from the first appearance of the ascites.

According to Coyon and Debray, who record a case of post-dysenteric polyneuritis, *nervous complications* in dysentery are not very rare, several examples having been published during the war and long before then (see *Medical Supplement*, 1918, **1**, 253). The present case occurred in a girl aged

19 admitted to hospital with paraplegia of four day's duration following an attack of Shiga bacillus dysentery. On admission there was typical flaccid paraplegia of the lower limbs, with loss of reflexes and pain on pressure on the muscles. In the upper limbs there was paresis and atrophy of the Aran-Duchenne type of the interossei and thenar and hypothenar eminences. Complete recovery gradually took place.

Commenting on the recent paper by Glaessner on *pancreatic disturbance* in dysentery (see *Medical Science*, 1921, **4**, 401), von Friedrich, of the Frankfort University Medical Clinic, states that he examined 20 cases of bacillary dysentery, 10 of which were acute and 10 chronic, but without finding any evidence that gastric achylia was accompanied by pancreatic achylia, or that the dysentery toxin damages the pancreas in a specific manner as apparently it does the stomach. According to von Friedrich the diarrhoea and dyspepsia in dysentery are not due to hypochylia of the pancreas. The diarrhoea is either the result of affection of the small intestine associated with gastric achylia or to infection of the small intestine from the large intestine. In any case lesions of the pancreas in bacillary dysentery, if they do occur at all, are very rare. Grote is quoted as having seen only two examples among a large number of cases of dysentery.

Treatment. According to Hausmann, of Moscow, the only rational treatment of dysentery is a rigorous and systematic method of purgation. A complete evacuation of the large intestine should be effected by frequent doses of Glauber's salts preceded by large doses of calomel. Constipating drugs, especially opium, should be avoided, as in typical dysentery constipation is present. Astringents are unnecessary. Absorbents such as animal charcoal are uncertain in their action and superfluous when energetic purgation is carried out.

Bernheim and Rosenblatt attach most importance to general treatment (rest, warmth, and diet), and from their experience of polyvalent and Shiga-Kruse serums injected intramuscularly or subcutaneously in doses of 40–80 c.cm., have come to the conclusion that they are of value in cases of moderate severity, but that, as similarly good results have been obtained by the use of normal serum (Czyhlarz and Neustadl, Kolle and Dorendorf), their action cannot be regarded as specific.

Lantin treated 105 cases of bacillary dysentery admitted in 1918 to the Philippine General Hospital, at Manila, by antidysenteric serum, with 12 deaths—a mortality of 10·47 per cent. as compared with a mortality of 17·8 and 20 per cent. respectively among 191 male and 71 female dysentery cases admitted to the hospital in 1912–13, when serum was not given. The following methods of administering the serum were used: (1) By rectum alone in doses of 30–80 c.cm. daily (9 cases); (2) by rectum and intramuscular injection combined (10 cases with 2 deaths); (3) intramuscular injection alone in doses of 20 c.cm. every four hours for the first three days, and 20 c.cm. twice a day thereafter; (4) intramuscular and intravenous injection combined (13 cases with 5 deaths); (5) intravenous injection alone in doses of 10–20 c.cm. daily (9 cases). The rectal administration of serum was of great advantage only when the patient was able to retain the serum for a long period. 24 hours after intrarectal injection the patient feels a marked alleviation of subjective symptoms, the colicky pain and tenesmus are diminished, the stools decrease in number, and the temperature falls. In the succeeding days the stools become less bloody and mucoid, and gradually become faeculent and of soft consistence. The intravenous method produces more rapid effects than intramuscular injection, but should be used with caution owing to the danger of embolism. The method of combined intramuscular and intrarectal injection appeared to be the most satisfactory.

Lornie and Jones report ten cases of asylum dysentery which were treated with a serum prepared by injecting horses with cultures of Shiga's, Flexner's, and Kruse's bacilli. Apart from the rapid clearing up of the blood and mucous and the cessation of diarrhoea, rapid fall in temperature and immediate and marked physical improvement were the outstanding features of the treatment.

De Biehler, of Warsaw, maintains that serotherapy, whether specific or polyvalent, is the most valuable method for treating dysentery, her experience being based on 129 cases in patients aged from 4 months to 19 years. In all but 16 cases in which a Shiga-Kruse or Flexner serum was used, a polyvalent serum was injected. With the exception of 3 fatal cases, considerable improvement in the general condition and character of the stools took place within 24 hours of injection.

On the other hand, Josephs and Davison, of Baltimore, during the last two years, have treated 20 children suffering from bacillary dysentery with polyvalent antidysenteric serum in doses of 20–50 c.cm. intramuscularly or subcutaneously, but without influencing the mortality or course of the disease. Davison also employed bacteriolytic filtrates active against one or more strains of Flexner bacilli in 12 cases of Flexner dysentery in children aged from 2 months to 4 years. The doses of the filtrates, which were given by mouth or rectum, ranged from 5 to 1,381 c.cm. This method also had no effect on the course or mortality of the disease.

II. Amoebic Dysentery

Epidemiology. Stiles, Professor of Zoology in the U.S. Public Health Service, brings forward statistics showing that, on an average, soldiers who served in Europe during the World War were not infected with amoebic dysentery any more than certain other elements of the U.S. population, e.g. immigrants at Ellis Island, boys and girls in training schools, civilians and soldiers who did not go to Europe. He is of opinion that the carrier of amoebic dysentery is not such a menace to his neighbours as has been supposed. He points out that the intensive studies on intestinal protozoa conducted during and since the World War bring out two practical points very clearly: (1) in temperate climates, at least, the intestinal protozoa are by no means of such clinical importance as had been feared or even assumed. Stiles does not believe that a routine examination for intestinal protozoa or worms is called for in every case of disease, but maintains that it is only in tropical and subtropical countries that this expense can be justified as a matter of administration. (2) In temperate climates at least, *Entamoeba histolytica*, the parasite of amoebic dysentery, is not usually a serious parasite, and its presence in healthy carriers is common.

According to Morin, of the Lausanne Medical Clinic, amoebic dysentery with its hepatic and pulmonary complications was rare in Switzerland before the War, but became widely diffused among the Swiss troops in 1914–18 owing to the presence of interned prisoners of war who were infected with amoebiasis.

Spolverini, director of the Cagliari University Institute of Clinical

Paediatrics, states that amoebic dysentery, which, up to four or five years ago, had been confined to a very few parts of Italy, such as Calabria and Sardinia, has recently invaded parts of the country which had hitherto been immune, without sparing any age, the infection being spread by soldiers suffering from acute or chronic dysentery or by healthy carriers. There is thus a repetition on a small scale of what has occurred in the cases of tuberculosis and malaria.

Symptoms. Several writers have recently drawn attention to *atypical forms* of amoebic dysentery which are liable to lead to errors in diagnosis. Thus Izar (1) (2), of the Catania University Institute of Medical Pathology, records cases simulating pulmonary tuberculosis, appendicitis, malaria, and typhoid fever. Paranhos and Reis describe five cases resembling mucomembranous enteritis, gastro-intestinal dyspepsia, acute periodic enteritis, and chronic enterocolitis. Carrau, of Montevideo, reports a fatal case of hepatic abscess in an infant of 20 months, mistaken for empyema. There was an absence of any intestinal history, and no ulcers or cicatrices were found in the intestine *post mortem*, but typical dysenteric lesions were discovered in the walls of the hepatic abscess.

Spolverini, who records five mild and almost chronic cases of amoebic dysentery in children aged from 2½ to 12 years, maintains that a search should be made for the *Entamoeba histolytica*, not only in all children with dysenteric symptoms, but also in those with obstinate anaemia.

Laporte and Roques report a case of *amoebic hepatitis* with a fever of an undulant type, of which no previous example has been recorded. A cure was obtained by injections of emetin hydrochloride.

Enneking, of Amsterdam, remarks that *hepatic abscess*, which is so frequent an occurrence in the tropics, is a very rare complication of indigenous amoebic dysentery in Europe. Caussade and Joltrain recorded the first case of the kind, which occurred in Paris in 1907. Chauffard, in 1913, reported two cases, one of which was in a man who had never left France but had been in close contact with colonials suffering from dysentery. Enneking records a case in a man who, without ever having left Holland, had suffered for eight years from colitis of unknown cause until examination of the stools showed the presence of *Entamoeba histolytica*. Two years later he developed signs of a commencing hepatic abscess which was successfully treated by emetin hydrochloride. Other examples of indigenous amoebic dysentery, complicated by hepatic abscess, have also been recorded recently by Cade and Rigal, of Lyons, in a boy aged 9, infected by his uncle, who had had dysentery at Salonica, and by van der Hoeven, in a woman aged 39, who had never been out of Holland.

Sanfilippo states that the frequency of *lesions of the appendix* in amoebiasis has been noted by several writers, such as Kartulis, Woolley and Musgrave, Harris, Hoppe-Seyler, Lenz, and Hogan. Henyer, in 49 autopsies on dysentery cases, found 7 with intestinal perforations; in 3 of these the perforation was situated in the caecum, in 2 in the appendix, and in 2 in the sigmoid. During life many patients complain of a pain localized in the right iliac fossa, and sometimes there is a typical attack of acute appendicitis, as in the cases recorded by Hoppe-Seyler and Le Roy des Barres. A true appendicitis may occur in the course of acute amoebiasis with actual lesions of the appendix, but this appendicitis is very often masked by the symptoms of dysentery or by those of general peritonitis due to perforation, and the condition is not discovered till the autopsy. In chronic amoebiasis, on the other hand, symptoms of chronic relapsing appendicitis may develop, although on operation or at the autopsy no anatomical lesion of the appendix is discovered. The symptoms in such cases appear to be of a reflex character, being caused by dysenteric lesions in the caecum.

Soca, of Montevideo, has found that whenever a dose of 8 cgm. of emetin hydrochloride has been repeated for several days in succession more or less marked toxic symptoms have appeared. He records a fatal case of *emetin polyneuritis* in a woman aged 37, who had received a total dose of 1·05 gm. emetin hydrochloride in the course of a fortnight. Eight days after the injections symptoms of polyneuritis developed, and death took place with bulbar symptoms after about six weeks' illness. There was no autopsy.

De Lavergne made a rectoscopic examination of four cases of chronic amoebic dysentery, in whose stools spirilla as well as amoebae were present, and found *ulcero-membranous lesions* exactly resembling those of Vincent's angina, the smears showing the characteristic symbiosis of spirilla and fusiform bacilli. He points out that this rectal localization of fuso-spirillar infection, like all the other localizations on the skin or mucous membranes, represents a superadded secondary infection which can develop only on already affected tissues like the rectal mucosa in chronic amoebic dysentery. The existence of this rectal localization of the fuso-spirillar symbiosis is of therapeutic interest. The resistance of some cases of amoebiasis to emetin is explained not merely by the presence of certain parasites, such as *Lamblia* or *Cercomonas*, which are present at the same time as the amoeba, but the same effects may be produced by the fuso-spirillar symbiosis, and in such cases treatment by arsenobenzol is specially indicated.

Dumont records two cases of amoebo-spirillar dysentery which were characterized by their chronic character and resistance to emetin. In one of the cases arsenobenzol did not cause any change in the clinical condition or in the bacteriology of the stools, while in the other it produced a rapid cure. Dumont also reports a case of chronic dysentery which was exclusively spirillar. Slow improvement followed intravenous injections of novarsenobenzol in doses of 0·30 gm. Recovery took place in a month's time, but the stools, which were normal in appearance, still contained spirilla.

Treatment. Mühlens and Menk, of the Hamburg Institute of Tropical Hygiene, found yatren—a compound of iodine 5 parts, oxychinolin 8 parts, sodium sulphate 4 parts—an excellent adjuvant in the treatment of chronic amoebic dysentery. It exerts a well-marked bactericidal action without damage to the tissues and also acts as a cell stimulant. Further observations and experiments, however, are required to determine if it has a permanent effect or specific action. A rectal injection of a 1·5 to 5 per cent. solution is given after the bowel has been washed out, and is retained as long as possible. The drug is also given in capsules of 1 gm. three times a day. This treatment is continued for one or two weeks, and after a week's interval for three to seven days. Mello, a Brazilian writer, records six cases treated by this method with successful results and without any toxic symptoms developing.

Macgregor and Frew have treated fifteen cases of amoebic dysentery at the Ruchill Fever Hospital, Glasgow, by the oral administration of alcresta combined with hypodermic injection of emetin. One tablet of alcresta, which contained the alkaloids (emetin and cephaëlin), from 10 grains of ipecacuanha U.S.P. was given thrice daily along with a hypodermic injection of emetin

(1 grain) daily for ten days. After an interval of a week a similar course of treatment was given, followed, if necessary, by a third course after a week's interval. The drug was in all cases well borne by the patients. In all the improvement during treatment was marked and rapid, and all with one exception had normal or microscopically negative stools on discharge from hospital. The benefit, however, was short-lived owing to the occurrence of relapses.

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J. D. R.

POST-OPERATIVE JEJUNAL ULCER

Despite the general improvement which has taken place in the results of operation for gastric and duodenal ulcer with diffusion of knowledge of the consequences of various methods of intervention, the appearance of a secondary ulcer at the line of anastomosis or in the neighbouring portion of the jejunum is, and for the present appears likely to remain, a most unsatisfactory complication in the otherwise favourable outlook.

The development of secondary ulceration in the alimentary canal on the distal side of a short circuit is not confined to the jejunum, an instance of ulceration of the colon below an anastomosis to the small intestine having been recorded by Pauchet (*Medical Science*, this number, p. 295). Nor would the jejunum appear entirely innocent of a tendency to develop simple ulcer without previous anastomosis to the stomach, Walton (*Medical Science*, 1922, **7**, 139) and Richardson (*Medical Science*, 1922, **7**, 140) having reported cases belonging to this category. The latter observer was able to collect 12 examples of this condition from the literature, though, owing to brevity of clinical reporting, an underlying basis of syphilis could scarcely be excluded.

Apart from the various debatable factors, mechanical, vasomotor, or nervous, which have, at various times, been brought forward as contributory causes of post-operative jejunal ulceration, there is a general agreement that the main aetiologic element is contact of acid gastric juice with the jejunal mucosa. A singularly apt illustration of this factor is afforded by a case recently reported by Holzweissig (*Medical Science*, this number, p. 293). The patient, who had suffered from gall-stones for many years, had one of her usual attacks of jaundice which, at the end of 24 hours, culminated in an obvious perforative peritonitis. The abdomen contained a large quantity of acid fluid which was escaping from a perforation in the first coil of the jejunum. At autopsy there was extensive ulceration of the first 10 cm. of the jejunum and occlusion of the bile papilla by an impacted gall-stone. Gastric juice had passed directly into the jejunum without neutralization by the bile and pancreatic juice, which were held up by the gall-stone. Microscopically the jejunal ulcers were free from round-cell infiltration and apparently of very recent formation.

Of the alternative types of gastro-jejunostomy available none is entirely free from the possibility of this complication, which, disabling at all times, may on occasion assume the dimensions of a catastrophe. Jejunal ulcer has been recorded after gastro-enterostomy, with or without pyloric occlusion, and after partial gastrectomy, whether completed by the Billroth II or Polya methods, or by Y-anastomosis. As would be expected, the Billroth I method of gastro-duodenal anastomosis offers apparently complete freedom from this complication, but is limited in its applicability by the technical difficulty of bringing together stomach and duodenum after a free resection of either viscus.

The proportion of cases in which secondary ulceration follows simple gastro-enterostomy is usually stated to be about 1·0 to 1·5 per cent., but there is room for doubt as to whether careful search would not reveal its presence in those comparatively frequent cases in which pain after operation is ascribed to persistence of the original ulcer, to adhesions, to appendicular dyspepsia, or even to the development of a neurosis. Taking anastomotic and jejunal ulcers together, the chief symptom, pain, may occur at any time, from immediately after the operation up to two years later. Development of symptoms more than two years after gastro-jejunostomy is rare, though v. Haberer (*Medical Science*, this number, p. 291) has recorded a case which was certainly free from pain for five years after a partial gastrectomy. The pain is similar to that associated with gastric ulcer, although occasionally a patient is more comfortable with a full than with an empty stomach. The more severe sequelae of secondary jejunal ulceration are haemorrhage, acute perforative peritonitis, perforation into the abdominal wall, and the formation of a jejuno-colic fistula.

Examination of the type of operation which is most often followed by secondary jejunal ulceration brings out at once the striking part played by artificial obliteration of the pylorus, by whatever method achieved. In this connexion the figures given by v. Haberer from his own series are illuminating. After 275 simple gastro-enterostomies there were 3 cases of jejunal ulcer, after 71 gastro-enterostomies with pyloric occlusion there were 12 cases of jejunal ulcer. Sherren states that a far greater number of jejunal ulcers followed his gastro-enterostomies performed during the two years in which he practised pyloric occlusion than appeared in his results before or after this period.

According to v. Haberer, it is solely the influence of pyloric occlusion which determines the apparently greater frequency of jejunal ulcer after gastro-enterostomy when performed for duodenal ulcer than after the same operation performed for gastric ulcer.

After simple gastro-enterostomy there is a considerable reduction in the total gastric acidity as measured by a test meal. Paterson gives the average reduction as 30 per cent. This reduction of acidity is due to neutralization of acid gastric juice by alkaline pancreatic juice regurgitating through the stoma, and is therefore dependent on the proper functioning of the mechanism for production of pancreatic juice. The excitation of pancreatic secretion is normally initiated by passage of acid through the pylorus. By contact of this acid with the duodenal mucosa is produced secretin, the hormone which is carried by the blood-stream to the pancreas, where it stimulates the secretion of pancreatic juice.

X-ray examination of an opaque meal after gastro-enterostomy shows that food still continues to pass through the pylorus and the ordinary secretin mechanism is therefore still active. Occlusion of the pylorus, however, necessarily cuts off the normal immediate supply of secretin and makes it dependent on contact of acid with the mucous membrane of the jejunum below the stoma. It is possible that the latter mode of production of secretin is not so effective or so immediate in the excitation of pancreatic secretion and so of neutralization of the gastric juice in the immediate neighbourhood of the stoma.

Galpern (*Medical Science*, this number, p. 292) in this connexion draws attention to the resemblance between the conditions obtaining after gastro-enterostomy with pyloric occlusion and those established experimentally by Popielski in his demonstration of the stimulation of pancreatic secretion by passage of acid through the pylorus into the duodenum. Popielski, working in Pawlow's laboratory, divided the stomach into cardiac and pyloric parts and established a fistula into each. Introduction of acid into the cardiac portion was not followed by secretion of pancreatic juice, whereas introduction of acid into the pyloric portion excited a normal flow of pancreatic secretion as soon as the acid had passed through the pylorus into the duodenum.

Now that pyloric occlusion, owing to recognition of its tendency to produce jejunal ulcer has fallen into a well-merited disuse, attention has been focused on methods of reduction of gastric acidity more reliable, in their achievement of the desired result, than the simple gastro-enterostomy. The acid of the gastric juice is produced by the cardiac glands, which were shown by Edkins to be activated by a hormone produced by contact of the first products of digestion resulting from the action of the appetite juice on the mucous membrane of the pyloric end of the stomach.

It is, therefore, clear that reduction of gastric acidity can be effected by operation in two ways, either by allowing neutralization by alkaline pancreatic juice regurgitating through a gastro-enterostomy stoma, the pylorus being intact, or by removal of the pyloric antrum, thereby interfering with the supply of acid at the source. In this type of operation, i. e. partial gastrectomy, completed by any form of gastro-jejunostomy, the secretin mechanism for stimulation of pancreatic juice is activated by contact of gastric juice with the mucous membrane of the jejunum, and if gastric acidity is reduced to the degree claimed by the more whole-hearted advocates of this operation it appears probable that pancreatic digestion must be considerably diminished among their patients.

The reduction of gastric acidity by removal of the pyloric antrum has been advocated recently by Lorenz and Schur (*Medical Science*, 1922, **7**, 138), following the experimental work of Gross and Krzyschowski on the greater reduction of gastric acidity after antrectomy than after gastro-enterostomy in dogs, and its confirmation in man by Schur and Plashke and by Kelling.

The comparative rarity of jejunal ulcer after partial gastrectomy, whether completed by the Billroth II or Polya methods, is apparent in any large series of post-operative results, e. g. v. Haberer (*Medical Science*, this number, p. 291) records 3 jejunal ulcers after 275 gastro-enterostomies, 1 jejunal ulcer after 391 gastro-duodenectomies. Lorenz and Schur, in their investigation of the degree of gastric acidity remaining after partial gastrectomy in man, find an absence of free HCl after complete removal of the pyloric antrum and a reduction proportional to the amount of antrum removed in the less radical operations. Owing to variations in the boundary between pyloric and cardiac glands it is necessary to remove from one-half to two-thirds of the stomach to ensure an absence of free HCl after operation. Finsterer has adopted a similar procedure and reports good results from antrectomy, but the operation has not yet been practised for a sufficient length of time or on a sufficient number of cases to allow of any estimate as to its ultimate effect in the elimination of post-operative jejunal ulcer.

That its success is likely to be but relative is suggested by the number of sporadic cases of jejunal ulceration reported by various surgeons after partial gastrectomy, a number now so considerable as to lead v. Haberer and v. Eiselsberg to avoid the gastro-jejunal short circuit altogether and return to the gastro-duodenal anastomosis (Billroth I).

The digestive effect of the gastric juice on the mucous membrane of the jejunum is, to some extent, under control, not only through the technical details of operation, but also through regulation of the post-operative diet. Too early resumption of solid food or of tempting dishes potent to excite appetite juice is generally recognized as a predisposing cause of jejunal ulcer.

Among the mechanical factors which have been accused of playing a part in the causation of jejunal ulcer may be mentioned compression by clamps and irritation by non-absorbable sutures. 'Clamp ulcers' of the stomach invariably heal, but necrotic areas of jejunal mucosa, whether produced by the direct pressure of clamps or indirectly through formation of a haematoma in the jejunal wall, may assume the characters of a chronic ulcer. For this reason Sherren has discarded the jejunal clamp during gastro-enterostomy.

Considerable attention has, of recent years, been directed to the rôle of the non-absorbable suture in the production of jejunal ulcer, and so many cases have been recorded in which a thread or silk stitch has projected through the floor of the ulcer into the lumen of the bowel that a causal connexion between ulcer and stitch can scarcely be doubted. This factor in the causation of jejunal ulcer can be, and has now largely been, abolished by the employment of catgut only for the suture material.

Beer, T. Beitrag zur Aetiologie des peptischen Jejunalgeschwürs. *Zentralbl. f. Chir.*, 1922, **49**, 282–4.

Galpern, J. Über die Entstehung von Ulcus pepticum jejuni nach Pylorusausschaltung nach v. Eiselsberg-Doyen. *Zentralbl. f. Chir.*, 1922, **49**, 519–21.

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E. K. M.

ABSTRACTS

SURGERY

CUSHING, HARVEY. The cranial hyperostoses produced by meningeal endotheliomas. *Arch. Neurol. & Psychiat.*, 1922, **8**, 139–54.

Cushing sets out to establish his view that the cranial hyperostoses overlying meningeal endotheliomas are the result of the subjacent tumours, and not, as Spiller stated, their cause. Areas of cranial thickening discovered by palpation or by X-ray are to be suspected of overlying meningeal endotheliomata. On the intradural aspect these tumours may be of two types: (1) massive tumours with small meningeal attachment, and (2) tumours en plaque, flat but involving a large mass of dura. It is in the second case that the overlying hyperostosis is apt to be most pronounced; in many cases the intracranial symptoms of tumour are due rather to the hyperostosis than to the endothelioma, which may attain large size before causing general pressure symptoms. He reports the case of a left temporosphenoidal endothelioma en plaque, with invasion and thickening of overlying bone and extracranial involvement of temporal muscle; the patient was a woman of 39 years,with bony tumour of the orbit producing exophthalmos. There had been an indefinite prominence of the left eye for 10 years; in 1919 the left eyelid became oedematous, and in 1920 (February) swelling of the temporal fossa was observed. In May 1921 the hyperostosis, together with underlying dura and its subjacent flat tumour, was extirpated. Ten months later the exophthalmos had subsided and there was freedom from symptoms.

On histological examination the muscle and the bone were found to contain tumour cells arranged in endothelial alveoli and the whorl-arrangement characteristic of dural endotheliomata.

Incidence. In his histologically verified cerebral tumour cases Cushing has found endothelioma 80 times and glioma 312, i. e. 10·7 per cent. of his brain tumours have been endotheliomas. (Frazier, in *N. York State J. M.*, 1921, **21**, 369, has stated that 60 per cent. of his cases were sarco-endotheliomas and only 38 per cent. gliomas.)

Hyperostosis cranei. 20/80ths of the endotheliomas were accompanied by recognizable thickening of the overlying bone. Endotheliomas en plaque are proportionately more often so associated with bony involvement than are large rounded tumours; most flat tumours have produced an overlying hyperostosis. Cushing suggests the name meningothelioma or meningioma for these tumours, for he and Weed believe that essentially they are of arachnoid rather than of dural origin, and that they are mesotheliomas. The overlying hyperostosis cranei is due to invasion of the bony canals by tumour cells, with resultant stimulation of osteoblasts and new bone formation.

In the following discussion Spiller emphasized the importance of the probability that where a large localized bony growth of skull is seen there is an underlying dural tumour. C. C. C.

Haberer, H. Termino-laterale Gastroduodenostomie bei der Resektionsmethode nach Billroth I. [**Termino-lateral gastro-duodenostomy in resection by the method of Billroth I.**] *Zentralbl. f. Chir.*, 1922, **49**, 1321–6.

Háberer records a case of jejunal ulcer following duodeno-pylorectomy for duodenal ulcer by the Billroth II method. He performed the first operation in 1915, and at a second in 1922 removed the anastomosis with a large part of the pyloric end of the stomach, completing the operation by an end-to-end jejuno-jejunostomy and a termino-lateral gastro-jejunostomy. The immediate result was satisfactory.

The occurrence of this case in his series of 391 cases of partial gastrectomy by the Billroth II method inclines Haberer to return to the Billroth I method. He refers to the risk of giving way of the suture line when the duodenum has to be cut through to the right of the level of peritoneal reflection. This risk he avoids by termino-lateral implantation of the cut end of the stomach into the anterior peritoneal covered surface of the duodenum, the latter being mobilized if necessary by a peritoneal incision along its convexity, as for exposure of the common bile-duct.

One disadvantage of mobilizing the duodenum is the possible formation of a haematoma, especially when a duodenal ulcer has produced much periduodenitis. A second disadvantage is that vomiting of bile is frequent during the first few days after operation. Apart from these two points, the cases behave exactly as after a typical Billroth I resection. Haberer has carried out this procedure in 17 cases with one death from giving way of the suture line in a patient who lost much blood in consequence of mobilization of the duodenum. E. K. M.

Arnsperger, L. Retrograde Dünndarminvagination nach Gastroenterostomie. [**Retrograde invagination of the small intestine after gastro-enterostomy.**] *Zentralbl. f. Chir.*, 1922, **49**, 190–2.

A case of a woman who, 11½ years before, had been operated on for pyloric ulcer. A posterior gastro-enterostomy was performed, followed 8 days later by entero-anastomosis on account of 'vicious circle'. In the following year she had three slight attacks of gastric colic, without vomiting, which were successfully treated by massage. She then remained free from symptoms for 10 years.

The illness which led to Arnsperger's interference commenced suddenly with epigastric colic and coffee-ground vomiting. The abdomen was soft, with ill-defined resistance in the left hypochondrium. A retrograde invagination of the jejunum immediately distal to the gastro-enterostomy was found, the whole tumour being 20 cm. in length. The apex of the invagination lay opposite the entero-anastomosis. Reduction was difficult, but the bowel was viable. Neither anastomotic opening showed anything unusual. Convalescence was uninterrupted. References are given to cases recorded by six other authors.

Arnsperger suggests that the 'vicious circle' symptoms for which entero-anastomosis was performed 8 days after the original gastro-enterostomy were possibly due to a minor degree of the condition found at operation 11 years later. E. K. M.

Beer, T. Beitrag zur Ätiologie des peptischen Jejunalgeschwürs. [**Contribution to the aetiology of peptic ulcer of the jejunum.**] *Zentralbl. f. Chir.*, 1922, **49**, 282–4.

The case recorded by Beer is that of a man, aged 29, who had suffered from gastric symptoms for 4 years. At laparotomy a duodenal ulcer was invaginated, and a posterior gastro-enterostomy performed. At the same time the pylorus was constricted by tying the ligamentum teres round it after incision of the sero-muscular coats. One year later there was recurrence of the pain and haematemesis. X-ray palpation showed a tender spot at the anastomosis.

At a second operation a round ulcer was found in the distal loop of the jejunum, 1 cm. from the gastro-enterostomy opening. The pylorus was patent. The region of the anastomosis was excised and the jejunum united by end-to-end suture. The pyloric antrum was removed and the open end of the stomach joined to the side of the jejunum beyond the jejunal anastomosis. Pain recurred in three weeks and gave rise to the suspicion of subphrenic abscess. The left subphrenic space was explored by rib resection, but found to be free from infection. The patient died 4 weeks after the stomach operation, in spite of transfusion of blood for melaena.

At autopsy a jejunal ulcer was present immediately distal to the gastrojejunostomy opening. In the base of the ulcer was an eroded tributary of the left colic vein. The intestines were full of blood.

Beer points out that this case affords evidence against Kelling's view that removal of the pyloric antrum prevents the formation of a jejunal ulcer by abolition of the mechanism of activation of the secretion of the acid-forming fundus glands, but omits to state with any precision how much of the stomach was removed. He also remarks on the variation in the number of cases of jejunal ulceration reported by different clinics, and considers that this discrepancy may be dependent on differences in the degree of mechanical injury produced by the use of clamps in the practice of different operators. E. K. M.

Galpern, J. Über die Entstehung von Ulcus pepticum jejuni nach Pylorusausschaltung nach v. Eiselsberg-Doyen. [**The development of peptic ulcer of the jejunum after pyloric exclusion after the v. Eiselsberg-Doyen method.**] *Zentralbl. f. Chir.*, 1922, **49**, 519–21.

Galpern draws attention to the significance of the work of the Pawlow school in relation to any discussion as to the results of structural alteration of the pylorus. The mechanism of excitation of a flow of pancreatic juice by activation of the duodenal mucous membrane when gastric juice comes into contact with it is illustrated by the experiment of Popielski, who divided a dog's stomach into cardiac and pyloric halves and established a fistula into each. No pancreatic juice was secreted when acid was introduced into the cardiac pouch, but a strong flow was obtained as soon as acid introduced into the pyloric pouch passed through the pylorus into the duodenum.

He points out that the operation of gastro-enterostomy combined with pyloric exclusion reproduces this experiment with considerable fidelity, the stomach being converted into an equivalent of the cardiac pouch of the experimental animal. Since no acid gastric juice can get through the pylorus into the duodenum, activation of the pancreatic secretion by secretin is wanting and the normal neutralization of gastric juice before contact with the mucous membrane of the jejunum does not occur. Under these circumstances, any mechanical injury of the anastomosis or neighbouring portion of the jejunum is liable to result in the formation of a peptic ulcer.

E. K. M.

ALAPY, H. Ein Vorschlag zur Operation des postoperativen Jejunalulcus. [**A suggestion as to the operation for post-operative jejunal ulcer.**] *Zentralbl. f. Chir.*, 1922, **49**, 253-5.

A case report of a man, aged 48, who had had a gastro-enterostomy performed for duodenal ulcer 6 years before. For 4 years he had had recurrence of ulcer pain. At operation a stenosing scar of the duodenum and a jejunal ulcer opposite the gastro-enterostomy opening were found. Resection of anastomosis, end-to-end jejuno-jejunostomy, closure of the stomach, and pyloroplasty were done.

The patient died 7 days later from mediastinitis following rupture of an emphysematous bulla into the mediastinum. The abdominal contents were in a satisfactory condition.

Alapy pleads for the more frequent employment of pyloroplasty in the operative treatment of gastric and duodenal ulcer on the grounds that no case of jejunal ulcer has ever yet been recorded after this procedure, and laments that in the majority of text-books of operative surgery the operation is dismissed with a brief, if complimentary, reference. He recommends the original technique of Finney without clamps as being much more easy to carry out than the so-called improvements with clamps, the use of which renders mobilization of the duodenum necessary to a degree which is often difficult. He urges strongly that cases of jejunal ulcer following gastro-enterostomy should be treated on the lines adopted in the case he quotes, in order to restore the normal anatomical relations of the parts as far as possible.

E. K. M.

HOLZWEISSIG, M. Über peptische Geschwürsbildung im Jejunum. [**The formation of peptic ulcer in the jejunum.**] *Zentralbl. f. Chir.*, 1922, **49**, 864-6.

Holzweissig discusses very briefly the main determining factors in the production of jejunal ulcer and instances a case of his own as an example of the part played by the acid of the gastric juice.

A woman, aged 64, who had suffered from gall-stones for 12 years, developed a sudden attack of perforative peritonitis. Laparotomy showed many gall-stones in gall-bladder and common bile-duct, with one stone blocking the papilla. This had produced slight jaundice. In the first loop of the jejunum was a perforation. The peritoneal cavity contained 2–3 litres of fluid which gave an acid reaction. This was closed by suture, but the patient succumbed. At autopsy eight acute ulcers were present in the first 10 cm. of the jejunum and in the mesentery opposite were two firm fleshy masses. Microscopic examination showed an absence of round-cell infiltration in the bases and margins of the ulcers, suggesting that they resulted from rapid digestion. The mesenteric masses consisted of lymphocytes but did not present the characteristic structure of a lymphatic gland.

His reading of the case is that, owing to occlusion of the bile papilla by a stone, gastric juice came directly into contact with the jejunum without previous neutralization in the duodenum and produced the ulcers found by direct digestion of the jejunal wall. This explanation is borne out by the presence of so large a quantity of acid fluid in the peritoneal cavity at operation. E. K. M.

v. Haberer, H. Zur Frage des Ulcus pepticum jejuni auf Grund älterer und neuerer klinischer Erfahrungen. [**Peptic ulcer of the jejunum in the light of old and recent clinical experience.**] *Archiv f. klin. Chir.*, 1922, **119**, 712–65.

The cases of jejunal ulcer on which this paper is based are those which have been through v. Haberer's hands between the end of 1912 and the end of 1921. In all he has operated upon 30 cases, in 4 of which no radical operation was possible. In the remaining 26 cases, 30 operations of a radical type have been performed. He deals first with the former group of 4 cases, 2 of which died of peritonitis following perforation of the jejunal ulcer. Both of the other 2 perforated into the anterior abdominal wall after establishment of adhesions. One was treated by jejunostomy and has been traced for 8 years afterwards, the other was treated by separate implantation of the two ends of the divided jejunum into the stomach. This case was alive after 2¼ years. He mentions, but does not include in the series, one other case of jejunal ulcer following gastro-enterostomy and pyloric exclusion, done by himself, which died 5 months after the second of two operations, performed by another surgeon, for gastro-colic fistula.

Of the 26 cases in which he was able to carry out radical removal of the jejunal ulcer, symptoms of the latter appeared within 2 years of the original gastro-jejunostomy, except in one instance where an interval of at least 5 years elapsed.

He thinks that the jejunal ulceration follows immediately on the original gastric operation in many cases, though it does not, as a rule, give rise to the characteristic symptoms for about two years. He has seen jejunal ulcer recur immediately after an operation for its relief, but has rarely encountered recurrence after a longer period than 2 years. He therefore takes freedom of recurrence of symptoms for 2 years as indicative of operative cure.

Among the 26 cases in which radical treatment was attempted there were 3 deaths, in all of which there was haemorrhage from the original or from the jejunal ulcer. In 2 cases there was recurrence of the jejunal ulceration. Of the 23 surviving cases, 6 are well after 7–9 years, 3 are well after 2 years, and the remainder, though well, have been operated on during the last 2 years and cannot therefore yet be regarded as cured.

Of the total of 30 cases of post-operative jejunal ulceration, 18 followed gastro-enterostomy combined with closure of the pylorus, 12 followed gastro-enterostomy alone. In 23 out of the 30 jejunal ulcers, the original operation was done for duodenal ulcer, i.e. gastro-enterostomy with occlusion of the pylorus 16 cases, gastro-enterostomy alone 6 cases, resection of the ulcer with gastro-enterostomy 1 case. Jejunal ulcer is therefore associated chiefly with artificial occlusion of the pylorus. When it follows simple gastro-enterostomy its rate of occurrence is the same whether the operation has been done for duodenal ulcer or for ulcer of the pyloric region of the stomach. The greater frequency of secondary jejunal ulceration after operations for duodenal ulcer is therefore dependent on the frequency with which occlusion of the pylorus has been carried out for this condition in the past. v. Haberer himself has performed 71 gastro-enterostomies with pyloric occlusion. 12 of these afterwards developed jejunal ulcer. Among 275 simple gastro-enterostomies there have been 3 jejunal ulcers, and after 865 duodeno-gastrectomies no case of jejunal ulcer.

The chief cause of post-operative jejunal ulcer is artificial occlusion of the pylorus. Among other causal factors he considers that injudicious feeding after operation is of great importance, whether it acts through mechanical irritation or by keeping up a high degree of digestive acidity. He does not allow solid food for two weeks after operation. Circulatory and nervous disturbances may have some aetiological moment, but he is not sure that any of the recently recommended methods of prevention of jejunal ulcer are founded on a recognition of the basic cause of the condition. In this connexion he refers to Lorenz and Schur's advocacy of antrum resection (*Medical Science,* 1922, **7**, 138) and points out that the effect of removal of the pylorus in antrum resection has not been taken into account by these authors. He has seen one case of jejunal ulcer after resection and completion by the Billroth II method done by another surgeon, but could form no opinion as to how much of the antrum had been removed.

The treatment he advises for jejunal ulcer is excision of the gastro-jejunostomy and jejunal ulcer, removal of any portion of the stomach or duodenum containing an ulcer, together with the pylorus, and completion of the operation by a modification of the Billroth I method in which the end of the duodenum is closed and the open end of the stomach is anastomosed to the side of the duodenum on its anterior peritoneal covered surface. He has returned to the Billroth I method on account of the number of cases of jejunal ulcer which have been recorded after operation by the Billroth II and Pólya methods. In 360 Billroth I operations he has seen only one recurrent ulcer of the duodenum, and is inclined to think that, in this case, it was a duodenal ulcer which he had overlooked at the previous operation. He reserves gastro-enterostomy for those cases in which radical operation is inadvisable on account of the general condition of the patient, or on account of technical difficulties introduced by local conditions in the operative field.

E. K. M.

Pauchet, V. Ulcus peptiques postopératoires du côlon. [**Post-operative peptic ulcers of the colon.**] *Bull. et mém. Soc. de chir. de Par.*, 1922, **48**, 514–17.

Pauchet records the case of a woman of 40 who, one month after the establishment of a short circuit for acute intestinal obstruction, developed an irritating diarrhoea. This was followed by abdominal pain and haemorrhage from the bowel. A year after operation sigmoidoscopy showed ulceration of the rectum and lower colon. The ulceration was cured by undoing the anastomosis between small and large intestine and re-establishing the continuity of each.

It was not possible to determine the position of the opening with reference to the upper and lower ends of the small intestine. E. K. M.

Kelling, G. Zum Verschluss der Duodenalfistel nach Magenresektion. [**Closure of duodenal fistula after resection of the stomach.**] *Zentralbl. f. Chir.*, 1922, **49**, 779–80.

A case report of a man aged 59, who developed a duodenal fistula 12 days after partial gastrectomy for carcinoma (Billroth I). After failure of non-operative methods of treatment, a jejunal fistula was established by the Witzel method well to the left of the previous incision, the opening in the jejunum being 1 m. from the duodeno-jejunal flexure.

The patient was fed through the jejunostomy tube with the addition of sod. carb. and pancreatin to the food supplied. The fistula closed on the twelfth day and remained closed though feeding by mouth was commenced at once. The absence of regurgitation through the fistula of fluid introduced through the jejunostomy was checked by testing with carmine.

E. K. M.

Chaton. Ulcus de la petite courbure traité par la sympathectomie. [**Ulcer of the lesser curvature treated by sympathectomy.**] *Bull. et mém. Soc. de chir. de Par.*, 1922, **48**, 994–7.

Chaton records 3 cases of ulcer of the lesser curvature treated by gastro-enterostomy combined with ligature and division of the coronary artery and its accompanying plexus of sympathetic nerves. The results were good, but there is nothing in his communication to indicate that section of the sympathetic nerve fibres contributed in any way to the success of the operations.

Although the capacity of the stomach to withstand mutilation is phenomenal, deliberate interruption of the main vascular supply of a chronic ulcer suggests an attitude of mind in which temerity and optimism struggle for the mastery. E. K. M.

Tsujimura. Über die Ascaridiasis der Gallenwege. [**Round worms in the bile tracts.**] *Deutsche Ztschr. f. Chir.*, 1922, **171**, 398.

Round worms have been found in the bile tracts in 33 published cases, usually in association with gall-stones, but in 8 cases there were no stones present. Clinical differences from cases of cholelithiasis have not been noticed; pain of varying character, jaundice, fever, and rigors have been reported.

It has occurred most commonly in adults, but two cases were in children of 2 and 9 years respectively. Only fully-developed worms have been found, 13 to 25 cm. in length. The worm has most frequently been met with in the common duct, more rarely in the hepatic duct and the gall-bladder; either a solitary worm or larger numbers may be present; in one case as many as 66 were counted; they may be dead or alive. The gall-bladder as a rule shows little change. G. E. O. W.

Lussana, S. Contributo allo studio dei tumori della clavicola. Due casi di sarcoma con frattura spontanea. [**Contribution to the study of tumours of the clavicle; two cases with spontaneous fracture.**] *Arch. ital. di chir.*, 1922, **5**, 621.

Benign tumours of the clavicle, except perhaps chondromata, are rare, but hard fibromata, myxomata, angiomata, and even lipomata, presumably subperiosteal, have been described. Besides the usual endosteal and periosteal sarcomata, malignant tumours having the characters of telangiectases, of endotheliomata, and of simple but recurrent enchondromata are recorded. Metastases of all kinds are met with, sometimes under guise of osteomata, and appearing, like the thyroidal deposits, before the original growth has attained a size leading to recognition. Trauma has been noted as an antecedent, both of primary and of metastatic growths. Malignant growths are twice as common in the clavicles of males as of females, and there is a slight preponderance on the left side.

Diagnosis is generally simple, though mistakes may be made as to exact site. Exuberant callus and syphilitic osteitis are the two conditions most easily mistaken. In spite of removal of the whole bone and its periosteum with the tumour, recurrence is common and generalization is, as a rule, early. The tumours sometimes attain a great size and exert pressure very widely and severely.

Sarcomata are not very common, for the author could find but 112 cases in the literature. In both his cases spontaneous fracture occurred. In one, it was the first symptom, in the other the break had been preceded by severe pain in the arm for two months, but no swelling was noticed until a week before admission. One tumour was a central round-celled sarcoma, the other a fusiform-celled periosteal sarcoma. The ages of his patients were 64 and 66 respectively. E. R. C.

Sauerbruch, F. Die Extirpation des Femur mit Umkipp-Plastik des Unterschenkels. [**Extirpation of the femur with plastic reversal of the leg.**] *Deutsche Ztschr. f. Chir.*, 1922, **169**, 1.

This operation was conceived for those cases in which the removal of the femur had been accomplished or was necessitated by disease, while the distal half was intact. Under ordinary circumstances this situation would be dealt with by amputation through or just below the hip-joint, leaving the patient with a stump to which it would be difficult to fit an artificial limb.

Sauerbruch removes the diseased femur from the knee-joint upwards, either after turning up an anterior flap or through a lateral incision ; the tibia is exposed by a cut along its anterior border and the edges of this incision are turned back. Corresponding to the length of bone required to replace the femur, the leg is amputated at the appropriate distance above the ankle-joint, using a posterior flap of periosteum, muscle, and skin; a portion of the fibula is removed to form an intramedullary peg.

The leg is now reversed so that the tibia replaces the excised femur and its lower end is pegged to the bone or joint above, while the condyles of the tibia form the lower end of the stump with the popliteal artery running across it to gain its anterior surface. The posterior aspect of the former leg becomes the anterior surface of the new thigh. The muscle flaps are sewn up in layers and drainage-tubes inserted ; the stump is finally fixed by plaster of Paris in an abducted position.

This method Sauerbruch has used in two cases. The first case was that of a girl of 13 years of age who had had a fracture of the left thigh with suppuration 6 years before. On two separate occasions bone-grafting had been carried out to close the resulting defect in the bone and thereby obtain union, but without success. The limb was quite useless and there was shortening of 20 cm., 8 cm. being in the distal half of the limb from lack of growth. The whole of the lower half of the femur was excised and the stump of the upper end freshened; the reversed tibia was fixed to the latter by an intramedullary peg made from the fibula. The case healed with some suppuration and the intramedullary peg came away, but the final result was satisfactory.

The second case was that of a man of 41, who had had a spontaneous fracture of the upper end of the femur as a result of sarcoma. The femur was removed through the hip- and knee-joints, the leg reversed, and the lower end of the tibia fixed into the hip-joint. The patient did well except for suppuration in a haematoma, but the case was too recent for the final result to be available.

Sauerbruch suggests that the principle of this operation might be extended to the upper limb. G. E. O. W.

Fisher, A. G. Timbrell. A study of loose bodies composed of cartilage or of cartilage and bone occurring in joints. *Brit. J. Surg.*, 1921, **8**, 493–523.

These bodies may occur (I) in connexion with a pathological process affecting the joint—osteoarthritis, tabes, &c.; (II) in joints otherwise normal; (III) as synovial chondromata. Among those of Group I the detached osteophytes of osteoarthritic joints show a centre of cancellous bone (the lacunae of which, however, are empty) with a periphery of fibrocartilage invested with fibrous tissue. Group II comprises the 'classical' form; the loose body is found chiefly in the knees of young males, is usually single, circular or oval in shape, and the size of an almond. While their presence may give rise to *secondary* osteoarthritic changes in the joint, the bodies themselves are shown to be the result of an injury which has separated a portion of articular cartilage with or without some of the underlying bone. They grow by proliferation of hyaline cartilage until, in some cases, their origin is obscured; when such a body is incompletely detached or acquires a secondary adhesion to the synovial membrane the bone corpuscles may live and new bone may be laid down on the surface of the old. The loose bodies of Group III are true chondromata arising from the cartilage cells of the synovial villi (first demonstrated by Kölliker), but whether as a result of traumatism or chronic synovitis is not clear. They contain no bone, and may be free or pedunculated, single, multiple, or diffuse.

A further study of the bodies of Group II confirms the belief that cartilage cells are not (as formerly taught) destitute of powers of repair, and that the use of cartilaginous grafts in surgery is based upon sound principles. It also supports Hey Groves's contention that the osteogenic cells in the Haversian canals and cancellous spaces of an autogenous bone-graft actively proliferate only if the graft becomes to some extent vascularized by the ingrowth of capillaries from surrounding parts.

The author demonstrates that cartilage cells are capable of growth and repair. C. C. E.

Fisher, A. G. Timbrell. A contribution to the pathology and etiology of osteo-arthritis. *Brit. J. Surg.*, 1922, **10**, 52–80.

This paper is a sequel to the one abstracted above. The central area of a normal articular cartilage has no covering of perichondrium. The superficial cells of this area are not renewed from the deeper ones, but are themselves the source of the deeper cells. The lateral articular area is covered by an extension of the synovial membrane containing capillaries derived from the circulus articuli vasculosus of William Hunter. This lateral part is, therefore, better nourished than the central, and reacts to the cause of osteoarthritis by proliferation, while the central, poorly nourished part reacts by degeneration. The deeper stratum of an articular cartilage is nourished chiefly by lymph exuded from the vessels in the cancellous spaces beneath it; percolating along the meshwork formed by the matrix surrounding the cell groups, the central area of the superficial stratum is nourished by the synovial fluid and the lateral area by the circulus vasculosus.

A *typical* case of rheumatoid arthritis differs clearly from a typical case of osteoarthritis. In the former the inflammatory changes begin in the synovial membrane and the capsular structures. There is more muscular spasm and greater limitation of movement. A pannus of granulation tissue is thus permitted to spread over the articular surface, intra-articular ankylosis being the usual result. In true osteoarthritis changes in the synovial membrane occur later than those in the articular cartilage and the above form of ankylosis is rare.

'Osteoarthritis', it is claimed, 'does not constitute a disease *sui generis*, but rather the series of physiological or pathological changes that occur in a joint when it is subjected to prolonged or oft-repeated injuries either mechanical or toxic, but of a moderate degree of intensity.' There is (*a*) the traumatic form, the occurrence of which is often to be regarded as evidence of improper treatment of the original injury, and (*b*) that due to bacterial toxins either formed locally or brought from some distant focus. This form, which includes the senile cases, is not, at first, a degenerative process, but inflammatory. Foci of infection elsewhere in the body can be demonstrated in almost every case. If, instead of treating the affected joints only, these foci are recognized early and adequately dealt with, there is often great benefit and there may be cure. C. C. E.

Felix, W. Anatomische, experimentelle und klinische Untersuchungen über den Phrenicus und über die Zwerchfellinnervation. [**Anatomical, experimental, and clinical investigations on the phrenic nerve and the innervation of the diaphragm.**] *Deutsche Ztschr. f. Chir.*, 1922, **171**, 283.

Felix investigated, by means of serial sections, 9 human embryos, and came to the conclusion that the phrenic nerve gives no branches to the pericardium or to the costal or mediastinal pleura. It gives branches to the serous membrane on both sides of the central and also to the lumbar portion of the diaphragm; in the latter area it probably makes connexion with the sympathetic. The peripheral portions of the diaphragmatic serous membranes are supplied by intercostal nerves.

The phrenic nerve communicates with the sympathetic in the neck and beneath the diaphragm; in the neck, the connexion is not direct from the ganglia of the sympathetic trunk, but from a plexus over the apex of the lung; this plexus also receives spinal branches from the lower cervical and the first dorsal nerves. On the under surface of the diaphragm the serous endings of the phrenic nerve anastomose with the sympathetic, and possibly the motor branches make connexion with this system; this phrenic plexus is accompanied by paraganglia. There are non-medullated fibres throughout the trunk of the phrenic.

The diaphragm is supplied with motor nerves almost entirely by the phrenic, but Felix states that the slip from the last rib is supplied by the last dorsal nerve; this observation he supports by reference to development and to the occurrence of failure of this portion in some cases of congenital hernia of the diaphragm.

Variations in the origin, in its connexions with other nerves, and in its course are discussed, and it is concluded that the position of the nerve on the lateral border of the scalenus anticus instead of its anterior surface, the presence of an accessory phrenic, and the rare intrathoracic anastomosis between the phrenic and the vagus are the most important variations from the surgical point of view. There may be difficulty in finding the nerve and, when found, its section may not produce a complete paralysis of the corresponding side of the diaphragm.

The topography of the posterior triangle with reference to the phrenic is described, and it is concluded that the nerve should be sought above rather than below the omohyoid muscle.

The supposed sensory function of the phrenic nerve is discussed and found to be based on :

1. The referred pain in affections involving either surface of the diaphragm ; a long list of these is given.
2. Experimental irritation of the central end of the cut nerve producing pain in the shoulder, a rise of blood-pressure, reflex nasal respiratory movements, degeneration in the phrenic nerve after section of the posterior roots.
3. Phrenic neuralgia.

Felix investigated these matters to some extent himself. In 10 cases of phrenicotomy under local anaesthesia he stimulated the central end of the divided nerve, and in 9 there was pain over the shoulder and in the region of the clavicle ; the phrenic nerve itself was not anaesthetized before the section. Twenty-one cases of disease are mentioned in which the shoulder pain was present, and in one of these there was hyperaesthesia of the skin over the right shoulder. Phrenic neuralgia and its tender points he cannot associate entirely with the phrenic nerve.

Felix holds that the sensory function of the phrenic is bound up with its sympathetic connexions. Its sensibility differs from that of an ordinary peripheral nerve, such as the ulnar, in that the stimulation of the central cut end of the phrenic produces a pain referred elsewhere than to the endings of the nerve, while in the ulnar the pain is referred to endings of the nerve. The sensation of the diaphragm is therefore comparable to that of the viscera.

For operative purposes blocking of the phrenic in the neck or just above the diaphragm produces anaesthesia of the serous membranes on both sides of the central part of the diaphragm.

On account of the varieties of the phrenic, more especially the accessory phrenic, section of the nerve in the neck does not necessarily produce a complete paralysis of the diaphragm on the same side ; Felix has found that if the peripheral end of the nerve is pulled out of the thorax a length of 10 to 12 cm. can be obtained, and in many cases the accessory phrenic is torn out too ; this method was found to produce a more complete paralysis of the diaphragm and was not associated with the production of any serious symptoms. G. E. O. W.

Romani, A. Ricerche sperimentali sulla rigenerazione dei nervi periferici in rapporto con alcune modalità di lesioni traumatiche. [B.] [**Experimental researches on regeneration of peripheral nerves in relation to the type of trauma.**] *Arch. ital. di chir.*, 1922, **5**, 639.

In Donati's Clinic it was observed that the effects of war injuries of nerves varied according to whether the trauma took the form of plain division, compression, or contusion, or whether these traumata were associated with a searing effect such as would be produced by hot pieces of projectile. The experiments were made on rabbits, the sciatic nerves being superficially injured, or punctured, with a thermo-cautery.

Degeneration in the peripheral part seems under these circumstances to be early and complete; so much so that no evidence of attempts at regeneration are discernible. On the other hand, whilst some degeneration is to be seen above the lesion, regeneration is little delayed, and when it occurs does not show the exuberance of new-formed filaments or the multitudinous spirals, helices, tufts, rings, and other forms found in the sprouting axis-cylinders of a proximal end after simple division. The dichotomous filaments, when they reach the sheaths of the degenerate cylinders beyond the lesion, do not enter them, but twine or interlace around them.

E. R. C.

Cioffi, F. L' infezione malarica nei rapporti con l' infortunistica e con la chirurgia. [**Malarial infection in relation to accidental injury and to surgery.**] *Arch. ital. di chir.*, 1922, **5**, 533.

The author is not concerned here with the influence of an existing malarial infection upon the occurrence of accidents; or with its effect in preventing or prolonging the healing of wounds; or with the persistence symptoms, such as wound neuralgia, in the infected; but with the possibility of a recrudescence of long quiescent malaria as the result of trauma or of surgical operations. There has for long been recognized an effect of this kind following direct injury to the spleen or heavy blows over the splenic region, and indeed the evidence for it is copious. There is also a certain amount of ground for admitting that injuries to long bones are competent to reawaken infection. In both cases the rationale of the process is clear, since they are the haemopoietic organs, but it is important, from the medico-legal and accident-insurance aspects to know whether all traumata and simple operations can be held responsible. Cioffi has made inquiries from a large number of Italian hospitals to which numerous malarial subjects are admitted, on these points, and has found that in those clinics in which chloroform is used it is extremely common for simple operative procedures to be followed in a day or so by malarial attacks, but that in those in which chloroform has been abandoned nothing of the kind is observed. He has also made observations on 60 railway employees, who were known to have suffered from malaria, who were injured, and in whom there was at a later period evidence of a persistence of the parasites in the blood, and in none of them was an attack determined by the trauma even when it concerned the bones.

He concludes that, as far as evidence goes at present, trauma, unless directly to the spleen or splenic region, and possibly such as to injure the bone-marrow, is not to be held responsible for a recrudescence of malaria. Surgical operations of discretion, such as those for hernia and the like, required by assured workmen, can be undertaken with security in this respect so long as chloroform be not the anaesthetic agent. There is a general review of the literature.

E. R. C.

Diez, S. La sifilide terziaria post-traumatica nell' infortunistica. [**Post-traumatic tertiary syphilis in the accidentally injured.**] *Policlin.*, 1922, **30**, Sez. Chir., 375.

Besides the direct implantation of infection by or in wounds, and apart from the influence of active syphilis on the healing and progress of injuries, it is of importance, from the medico-legal and insurance aspects to recognize the effect of trauma in determining a recrudescence of latent disease. There is abundant evidence that every kind of trauma—contusions, wounds, burns, fractures, dislocations, even blisters and hypodermic injections—may provoke a local gumma, and that every tissue and organ may suffer. The author reviews the literature and cites many interesting examples, including experimental work of Tarnowsky and others. The most difficult cases are those affecting the nervous system, where the influence of physical trauma is complicated by a psychic element. Pathogenesis is not quite a simple matter. When the trauma affects directly the bone-marrow, where the spirochaete may be considered to be resting, and when a new invasion of the blood-stream results, or when the existing, if unstable, general immunity may be upset by shock, fresh manifestations of the disease may be expected. But when the result, as is usually the case, is a gumma at the injured site without lesions elsewhere in the body, a local loss of immunity must be postulated, and the innate protective powers of the tissues themselves invoked. Possibly the spironema, as some evidence goes to show, remains latent in other tissues than those of the haemopoietic system. There is also the question of the selection of the site of an old injury, callus or cicatrix, as the site of a syphilitic lesion due to a subsequently acquired infection. To establish causal connexion with the trauma, three elements must be considered: the nature of the trauma and the alterations produced by it in the tissues, the interval elapsing, the site of specific lesion, and the present state of the subject. As regards the interval, some put it as short as six weeks, some extend it to six months, and others see no clinical limit even when a legal limit exists. In any case it should be established that there was no pre-existing lesion at the site injured or active signs elsewhere. Estimation of diminished wage-earning capacity must be considered solely in reference to each particular case. In the case that the author records at length, a man who had never been treated for syphilis and had had only one doubtful lesion since, at 22, he had had three ulcers on the penis which were considered not to be specific; at the age of 42 he suffered a severe contusion over the condyle of his femur. An arthritis resulted by which he was incapacitated for many months; although the fluid from the joint was injected into a guinea-pig with negative results, he was submitted to arthrectomy in another clinic and obtained no relief from his severe nocturnal pains. Subsequently a trigeminal neuralgia led to a blood test, which was positive, and a course of neosalvarsan not only cured the neuralgia but also banished the bone pains forthwith, so that he returned to work. In this case, despite the 20 years' interval since infection, the direct sequence, the localization, and the character of the lesion established the causal connexion.

E. R. C.

NEUROLOGY

FRAZIER, C. H., and SPILLER, W. G. An analysis of fourteen consecutive cases of spinal cord tumour. *J. Am. M. Ass.*, 1922, **79**, 1024.

In thirteen of the recorded cases, pain was a constant and initial symptom, and in seven of the number had been the sole symptom for not less than two years. It was of constant localization in a given case, persistent and relatively unvarying in intensity, and aggravated by sneezing or coughing. The invariable second symptom was paraesthesia—that is, subjective sensory disturbance. While the pain was a root symptom, the paraesthesiae were signs of cord compression and were referred to one or both limbs. They were described as a sense of sleepiness or numbness, itching or tingling. In no one of the series was a typical Brown-Séquard syndrome present. In two cases the tumour was sufficiently high to involve an upper limb. In half the total both lower limbs were affected, in the other half a single lower limb only. The early motor symptoms were referable to spasticity rather than to weakness, and consisted of clumsiness of movement. The sequence of events is, therefore, pain, paraesthesia, and paresis. The majority of the tumours were situated laterally to the cord. Xanthochromia in the cerebrospinal fluid the authors found to be a late symptom, and therefore of no value for early diagnosis.

In localizing the level of the tumour, they find the important factors to be upper level of sensory change, point of referred pain, sympathetic phenomena, absence of a reflex, and muscular atrophy, in the order named. The cervical sympathetic provides the sympathetic symptom referred to.

In discussing surgical treatment, the authors make the following points: the level of the lowest lamina to be removed should correspond with the localization of the segment representing the highest level of sensory loss, and to prevent recurrence the operator should remove with the tumour that portion of the meninges from which it originated. F. M. R. W.

WOLTMAN, H. W. Malignant tumours of the nasopharynx with involvement of the nervous system. [B.] *Arch. Neurol. & Psychiat.*, 1922, **8**, 412.

Woltman records a series of 25 cases of nasopharyngeal tumour with symptoms referable to the nervous system, observed in the Mayo Clinic. He also gives a tabular summary of 44 similar cases from the literature. Pathologically considered, the growth was a squamous epithelioma in 15 cases and a lymphosarcoma in 6. It commonly arises near the orifice of the eustachian tube in the fossa of Rosenmüller, and in the cases under consideration extension is upwards towards the base of the skull. The bony structures in this neighbourhood are mostly thin and lamellar and easily eroded, and there are numerous foramina and fissures through which the growth may extend. The sphenoid and ethmoid are usually eroded early and the growth extends through the foramen lacerum, the sphenomaxillary fissure, the orbital fissure, and the orbital plates. In one case the pituitary fossa was invaded. Metastasis occurred in a single instance.

The neurological symptoms consist in cranial nerve palsies, the nerves being involved as they lie in fissures or foramina and not in their intracranial course. Thus they tend to be involved in groups simultaneously;

most frequently those entering the orbit are the first to be affected, but in other instances the jugular foramen group may be the first. The single nerve most often involved is the sixth. External rectus palsy may be the initial and for a time the sole neurological symptom. The fifth nerve is the next most frequently involved (sensory alone in 11, motor also in 6 cases). The sensory symptoms are pain, paraesthesia, and impairment of sensibility. The optic nerve is not rarely involved by intra-orbital growth with the production of optic atrophy and blindness. The seventh and eighth nerves were not involved in any of the present series, and deafness and tinnitus, when observed, were due to direct involvement of the eustachian tube by tumour. The ninth, tenth, eleventh, and twelfth nerves were commonly involved, but in some instances immobility of the palate is produced, as Trotter has pointed out (cf. *Medical Science,* 1921, **4**, 242), by local extension of the growth.

In nearly all the case records appended to the paper it is stated that the cervical glands were enlarged. In only one instance was a correct diagnosis—that is, one of nasopharyngeal tumour—made during life, and it would appear that the association of cranial nerve palsies with enlargement of the cervical glands is the condition which should lead the clinician to suspect the presence of this lesion. F. M. R. W.

Foix, Thévenard, et **Nicolesco.** Algie faciale d'origine bulbo-trigéminale au cours de la syringomyélie. Troubles sympathiques concomitants. Douleur à type cellulaire. [**Pain of bulbar origin in syringomyelia. Sympathetic symptoms. Pain of cellular origin.**] *Rev. neurol.,* 1922, **29**, 990.

The patient was a house-painter of 50 and suffered from phthisis. The malady now under discussion developed suddenly three years before death with paroxysms of severe neuralgic pain on the right side of the neck, face, and scalp. The attacks of pain grew in frequency, and in three months became almost continuous. The pain was described as superficial and burning and tearing in quality. It was brought on by exposure to cold, and was accompanied by extreme cutaneous hyperaesthesia over the affected area of skin. Later, similar symptoms developed on the left side of the head, but in less intensity. The skin of the right half of the face was flushed and the pinna cyanosed, and the temperature of the skin was above that obtaining elsewhere on the surface. Further, tear, saliva, and sweat secretion were more marked on the right side. There was no definite abnormality in the palpebral fissure or pupil on the right. No other evidence of a lesion of the nervous system was discovered. The patient succumbed to tuberculosis.

The brain, cranial nerves, and gasserian ganglia were normal in appearance on the surface. On section, the only abnormality found was a syringomyelic cavity extending from the lower half of the cervical down through the upper segments of the thoracic cord. On microscopic examination, the cavity was central and had displaced rather than destroyed the grey matter of the cord. The cord and medulla were hyperaemic. The nature of the wall of the cavity was that usually seen in syringomyelia. In the lower levels of the medulla on the right side was a fissure in the postero-external region occupying the situation of the substantia gelatinosa Rolandi and presenting the usual features of syringobulbia. The nerve-cells immediately surrounding the fissure showed some chromatolysis.

The authors point out that the case is of considerable interest in that it demonstrates the existence of trigeminal pain of bulbar origin, it gives a clear notion as to the characters of pain of central origin, and confirms the view of the cellular origin of pain arising in ganglia, brain-stem, and thalamus. The medullary fissure described occupied the position of the descending root of the fifth nerve. They emphasize that central pain is known to occur in cases of haematomyelia and syringomyelia, and that in this instance certain well-marked symptoms were present which are usually attributed to a lesion of the sympathetic. F. M. R. W.

TRUELLE AND OTHERS. Le traitement de la paralysie générale. [**The treatment of general paralysis.**] *Rev. neurol.*, 1922, **29**, 921.

In 1822, Bayle, in his inaugural thesis, published when he was 23, gave the earliest description of general paralysis as a clinical entity. The centenary of this important event was celebrated in Paris by a congress of neurologists and psychiatrists in May of this year, at which every aspect of the disease was discussed. Among the seven papers that of Truelle, with the discussion following it, is of the greatest practical interest. Truelle believes that at present general paralysis is an incurable disease. He reviews the various modes of treatment adopted, and from the oral administration of mercury to Wagner von Jauregg's malarial infection he attributes the results claimed, by each and every method, either to the ordinary remissions of the disease or to confusion with cerebral syphilis.

In respect of palliative treatment, he lays stress on general hygienic measures, but since all general paralytics are debilitated individuals he regards drug treatment as requiring considerable caution.

Sicard expressed the view that the arsenical compounds given by the intramuscular route may arrest the progress of the disease in its early stages, but do not cure it. Rodriguez (of Barcelona) employed intravenous arsenobenzol and intrathecal salvarsanized or mercurialized serum, and claimed 'satisfactory results'. Eight others present, including Lhermitte, Anglade, Béhague, and Klippel, regarded all forms of antisyphilitic treatment as ineffectual, when not actually harmful. F. M. R. W.

GOLLA, F., and HETTWER, J. The influence of various conditions on the time relations of tendon reflexes in the human subject. *Proc. Roy. Soc. B.*, 1922, **94**, 92.

The knee-jerk was the reflex chosen for investigation. Uniformity of stimulus was obtained by electrically released pendulums, and the response was recorded electromyographically by means of the string galvanometer. In these circumstances, the authors find that the magnitude of the response is influenced by the strength of the stimulus and by certain psychical and physical factors in the subject which lead to an increased tone in the reacting quadriceps (cf. *Medical Science*, 1922, **6**, 41). The latent period of the response varies inversely with the strength of the stimulus, and undergoes the most marked shortening when rhythmically repeated stimuli are employed. There is a refractory period, independent of the strength of stimulus evoking the jerk which gives rise to it, but varying inversely with the strength of stimulus used to determine it. They regard the knee-jerk as an 'all-or-none' response for each single neurone concerned in it. The muscles antagonistic to quadriceps enter into contraction 10 sigma (1/100 sec.) later than quadriceps. This contraction of antagonists forms part of the spinal reflex pattern elicited by tendon stimulation. F. M. R. W.

Spatz, H. Ueber eine einfache Methode zur anatomischen Schnelldiagnose der progressiven Paralyse. [**A simple method for rapid histological diagnosis of general paralysis.**] *München. med. Wchnschr.*, 1922, **69**, 1326.

Perivascular collections of iron-containing pigment are a characteristic finding in the cortical grey matter in general paralysis. Lubarsch found the condition in 100 per cent. of cases examined. Trypanosomiasis is the only other disease of which this can be said. Spatz describes a rapid and easy method for demonstrating the pigment. Thin pieces of fresh tissue from the frontal cortex and the cornu ammonis are placed in concentrated ammonium sulphide solution for 15 minutes and then washed in water. The cortex will now give a moderate iron reaction, namely, a grey-green coloration to the naked eye. In general paralysis, examination with a hand-lens reveals tiny dark areas in the cortex. One of these is picked out with a sharp-pointed glass rod and placed on a slide in a drop of glycerine. A cover-slip is then pressed upon the fragment so as to make a smear preparation. Under the microscope, tiny dark green-black particles are seen. These are fragments of blood-vessels. The appearance is quite characteristic and differs from the pigmentation seen after haemorrhages. Since, in stationary cases, these collections of iron pigment round vessels are not numerous, a negative finding in such cases must not be regarded as final. Spatz regards the method as sufficiently constant and characteristic to be employed as a routine method of diagnosis. F. M. R. W.

Meyers, I. L. Magnus and de Kleijn phenomena in brain lesions of man. A consideration of these and other forced attitudes in the so-called decerebrate man. *Arch. Neurol. & Psychiat.*, 1922, **8**, 383.

Two cases are recorded, one of cerebral sclerosis and one of cerebellar atrophy, in which rotation of the head evoked reflex changes of posture resembling the tonic neck reflexes described by Magnus and de Kleijn (cf. *Medical Science*, 1922, **7**, 109). The patients were both infants. They were semi-conscious and in strong extensor spasm with opisthotonos, head retraction, and involuntary movements of the upper limbs. The clinical details are not satisfactory, and the lengthy discussion on the clinical physiology of rigidity and postural reflexes is confused and inaccurate. The writer's acquaintance with the physiological work he quotes is evidently very incomplete. F. M. R. W.

Santy, P., et **Langeron, L.** États méningés consécutifs à la rachi-anesthésie. Essai de classification clinique et d'interprétation pathogénique. [**Meningeal reactions following spinal anaesthesia.**] *Lyon Chirurgical*, 1921, **18**, 23.

In this paper Santy and Langeron discuss the after-effects which sometimes follow the injection of an analgesic solution into the spinal theca. They use the vague term 'meningeal conditions' purposely to include cases of all grades of severity showing signs of meningeal irritation, inflammation, and infection. In this paper they do not concern themselves with spinal or ocular palsies such as are well known to follow in rare instances on the giving of a spinal local anaesthetic.

The authors describe various degrees of spinal meningeal trouble.

1. Slight meningeal reaction, characterized by headache, spinal pain,

and slight contracture of the limbs. This is relatively common, but was of a severer type in the early days when solutions of cocaine were employed for injection. Ravaut and Aubourg, and Guinard, are cited as having observed true aseptic meningitides in these cases, characterized by intense headache, increased tension in the cerebrospinal fluid, the presence of a leucocytosis, and spontaneous fibrinous coagulation of the fluid after lumbar puncture. Only once in 21 cases was the cerebrospinal fluid normal. With novocaine such results are much more uncommon, but none the less Mestrezat and Riche found even in these cases (10 examined) a constant reaction: slight increase of chlorides and sugar without increase in protein, and a very sparse lymphocytosis.

2. Spinal meningeal haemorrhage. Operation for osteoma of femur. M. 49. Following spinal analgesia with 0·12 cgm. of allocaine, the patient complained of violent occipital headache with slowing of the pulse to 54. Lumbar puncture three days later revealed blood-stained cerebrospinal fluid. During the next five days the fluid became first rose-tinted and then faint yellow. They are certain that this haemorrhage was not the result of the puncture.

3. Acute aseptic puriform meningitis.

After referring to a case reported by Pautrier and Clément Simon, they record a case of their own. Spinal analgesia with scurocaine, operation for vicious union of fracture of leg. M., aged 26. Within five hours the patient was comatose, breathing stertorously with slight rigidity of the limbs. Pulse 120. Spinal rigidity. Three lumbar punctures within 24 hours showed 'dirty' cerebrospinal fluid under pressure, extensive deposit of polymorphonuclears, no micro-organisms: culture sterile. On the third day he suddenly recovered. He was given injections of antistreptococcal and antimeningococcal serum: cultures always sterile: polymorphonuclear leucocytes diminished and then mononuclears appeared in the fluid during the three days of the meningeal reaction: sugar was not diminished (an important point), but there was hyperalbuminosis. On the fourth day the fluid was normal.

4. Hyperacute septic meningitis.

Operation for varicocele: young soldier with slight pharyngitis, hence spinal analgesia with allocaine. Thirteen hours later the patient complained of spasms in the limbs, and six hours later he became unconscious and died. Lumbar puncture withdrew cloudy cerebrospinal fluid from which *Micrococcus catarrhalis* was isolated. The authors deny the possibility of contamination at the time of operation.

The authors discuss the pathogenesis of the above conditions. To take the last case first. They believe that this is an example of haematogenous infection of the cerebrospinal fluid by an organism already in the blood. Their authority for this belief is, of course, Weed's work and that of the Neuro-surgical Service at Baltimore. The character of the organism bears out this view.

The other more usual cases Santy and Langeron believe to be examples of aseptic meningitis produced by chemical means (the drug injected). They believe that we have in these cases a lepto-meningitis of toxic origin, characterized by leucocytosis, rise of tension, hyperaemia, and even haemorrhage, but always aseptic. They refer to some interesting experiments made by Sicard and Salin, who injected novocaine solutions into the spinal theca of moribund patients and found later lepto-meningitis with perivascular diapedesis especially marked in the pia-arachnoid and about the posterior roots.

The authors conclude that the existence of these toxic meningitides is interesting in a general manner, for they may explain the meningeal haemorrhages sometimes found without obvious cause in young people. The reader may not be willing to accept the interpretations they adopt for the cases described. G. J.

PATHOLOGY

Cummins, S. L. The anti-bactericidal properties of colloidal silica. *Brit. J. Exper. Path.*, 1922, **3**, 237.

Colloidal silica has the property of interfering with the bactericidal power of blood in marked degree. It inhibits the action of 'complement' in a haemolytic mixture. This anticomplementary property is probably the character to which it owes its antibactericidal power. These properties, together with its want of any demonstrable germicidal power, point to colloidal silica as likely to be of great use in blood-cultures in cases of bacteriaemia. P. F.

Mottram, J. C., Cramer, W., and **Drew, A. H. Vitamins, exposure to radium and intestinal fat absorption.** *Brit. J. Exper. Path.*, 1922, **3**, 179.

The histo-chemical study of fat absorption from the intestine demonstrates that the functional activity of the intestinal epithelium as regards absorption is profoundly affected by the presence in the food of vitamins A and B, particularly the latter. These 'food-accessory factors' have a stimulating action on intestinal absorption, and probably also on intestinal digestion, even in quite normal animals which have not been subjected previously to any special diet. On the other hand, in the absence of vitamins there is no delay in the passage of food in such animals. After exposure to radium sufficient to produce a lymphopenia, the absorption of food is impaired in the same way as if vitamins were absent, and this effect cannot be counteracted by an abundant supply of vitamins in the food. The observations confirm the view previously expressed by the authors that lymphocytes play an important part in the absorption of food, and that the marasmus resulting from a deficiency of the water-soluble vitamin is due to an impaired absorption and assimilation of food from the intestine. P. F.

Gye, W. E., and **Kettle, E. H. Silicosis and miners' phthisis.** *Brit. J. Exper. Path.*, 1922, **3**, 241.

Insoluble silica and silica sol, injected subcutaneously, cause a similar and characteristic lesion consisting of a central area of necrosis surrounded by a zone of leucocytes; around this again is a second annular zone of necrosis limited by macrophages and granulation tissue. Tubercle bacilli proliferate rapidly in the necrotic areas, a small dose of bacilli becoming a large dose. In this way silica aids in establishing a local infection.

P. F.

Campbell, J. M. H. The relative volume of corpuscles and plasma, and the relation of this to haemoglobin percentage and the number of the red blood-corpuscles. *Brit. J. Exper. Path.*, 1922, **3**, 217.

A method is described for estimating accurately the volume of red corpuscles in whole blood. In normals this was found to be 40 per cent. The corpuscular volume varies almost directly with the haemoglobin percentage. There is little change in the concentration of haemoglobin in the corpuscle in various pathological conditions. P. F.

Henderson, Y., and Haggard, H. W. Haemorrhage as a form of asphyxia. *J. Am. M. Ass.*, 1922, **78**, 697–704.

Henderson and Haggard contribute a study of haemorrhage as a form of asphyxia in which they apply the recently gained knowledge of disturbance of the acid-alkali balance to the problems of haemorrhage. Their experiments were made on dogs bled to a constant amount which brought them to the verge of death. Transfusion of saline, acacia solution, &c., had at the best a transient effect. The authors assume (but submit no experiments of their own) that transfusion would have shown about 100 per cent. of recoveries. They deduce that the red cells must be the important factor in blood transfusion in virtue of their capacity as oxygen carriers. The clinical features of haemorrhage are similar to those of certain conditions produced by oxygen starvation, viz. CO poisoning, oxygen deprivation, and acclimatization to high altitudes. In particular, the amount of breathing is much increased. This in turn ventilates off a large amount of carbon dioxide, and alkali begins to disappear from the blood. Any cessation of this process is of good prognostic significance, but if it be not stayed the animal dies. From this point the precise significance of the acapnial process has yet to be elucidated, the war having interfered with the research. Henderson and Haggard reach the temperate conclusion that the widespread insistence on the circulatory factor in haemorrhage needs reconsideration in the light of their researches. G. W.

Fineman, S. A study of microlymphoidocytic leukaemia. *Arch. Int. Med.*, 1922, **29**, 168–220.

Fineman reports at length his studies of the cytology in a case of microlymphoidocytic leukaemia. He concludes that the majority of the abnormal cells present were such as would have been described as myeloblasts, or at least as of myeloid origin by dualists. Yet his histological studies seemed to show that these very cells were being formed in the germ centres of the lymph-glands. Fineman does not push the argument further, but is evidently not at all in sympathy with the position of dualists.

G. W.

Kofoid, C. A., Boyers, L. M., and Swezy, O. Occurrence of *Endameba dysenteriae* in the lesions of Hodgkin's disease. *J. Am. M. Ass.*, 1922, **78**, 1604–7.

Kofoid, Boyers, and Swezy, record the finding in the stools and lesions of various cases of Hodgkin's disease of cysts of '*Endameba dysenteriae*'. Much and detailed examination is required before cysts are found, and it

does not appear that they occur in any considerable numbers. No differential stain is effective, and the diagnosis has been based purely on the morphology, particularly of the nucleus.
G. W.

LOEPER, M. A propos de l'albuminose du sérum des cancéreux. [**On the albumins in the serum of cancer patients.**] *Presse méd.*, 1922, **30**, 321.

Loeper writes to refute the suggestion that the increase of the albumins which he has described as occurring in the blood-serum of cancer cases can be due to hepatic derangement. He does not deny that it may occur in various sorts of liver disease as well as in cancer, but affirms its existence in cases of cancer not affecting the liver. He further points out that the increase which occurs when tumours are irradiated can hardly be explicable by reference to the liver.
G. W.

GOIA, J. L'action de l'adrénaline sur le tableau leucocytaire dans les myéloses. [**The action of adrenalin on the leucocyte count in cases of myeloid leukaemia.**] *Presse méd.*, 1922, **30**, 366–9.

Goia has followed researches as to the action of adrenalin injections on the normal blood by submitting cases of myeloid leukaemia to a series of tests. His object was to ascertain whether the myeloid tissue reacted to adrenalin, and how far the contraction of spleen and glands might be a factor. He finds that adrenalin always produces a marked increase in the number of circulating myelocytes. These, of course, come from the spleen and glands as well as from the marrow. But the number appears (only three cases are reported) to bear some relation to the degree of involvement of tissues outside the marrow. The practical point emerges that adrenalin tends to bring into the blood-stream cells of an earlier generation than the usual inhabitants. In an aleukaemic case a positive reaction would suggest that leukaemia was present, a negative reaction would probably indicate Hodgkin's disease or some alternative diagnosis.
G. W.

FLÖYSTRUP, G. **Studies on the pathogenesis of auricular fibrillation.** *Acta Med. Scand.*, 1922, **56**, 12–32.

Flöystrup has carried out microscopic examinations of the hearts of 9 patients who had suffered from auricular fibrillation, and 6 hearts the auricles of which had not fibrillated. Cross-sections, 10 μ thick, of the sinus node were cut, and every tenth or fifteenth was examined after staining with haematoxylin-van Gieson or haematoxylin-eosin. Staining with Flemming's solution, safranin, and picric acid was also carried out, and the nerves and ganglia were examined after staining by Walter's and a modification of Weigert's method. Flöystrup supplements his own material with the records of 19 other cases examined in the same manner. He comes to the conclusion that it is doubtful whether the real cause of auricular fibrillation is to be found in disease of the sino-auricular nodes because (1) as great disease of these nodes was found in hearts which had not fibrillated, and (2) in some hearts, which had fibrillated, the microscopic appearance of these nodes was normal. With regard to dilatation of the auricles being a cause of their fibrillation, he notes that dilatation and fibrillation are frequent associates, but that there also may be dilatation without fibrillation, and fibrillation with auricles of normal size. Probably both anomalies are the consequences of a third factor, although dilatation also presumably disposes to fibrillation. In only 11·5 per cent. was the appearance of the muscles of the auricles normal; there were only slight changes in 19·2 per cent. Thus, in 11·5 per cent. plus 19·2 per cent. it is highly improbable that structural changes in the auricles could be responsible for their fibrillation. Among the controls without auricular fibrillation there were several cases with microscopic changes in the auricles. These changes do not, therefore, *per se*, induce fibrillation, although often associated with it. Every one of the auricles examined after a history of fibrillation showed signs of having had to work against an absolutely or relatively increased resistance. With regard to the provocation of transitory auricular fibrillation by functional anomalies of the nerves of the heart, Flöystrup argues that this certainly can happen because (1) such attacks may occur quite suddenly, without any disease of the heart or other occasion for the arrhythmia, (2) such attacks occur oftener than not as 'nervous palpitation of the heart', and (3) the arrhythmia may be experimentally produced by synchronous irritation of the vagus and sympathetic nerves in dogs (Rothberger and Winterberg). But in the case of chronic fibrillation, which is far more common than transitory fibrillation, the cause cannot be traced to a pathological function of the nerves because (1) there is nothing in these patients to suggest a neurosis of the heart, and (2) other anomalies are always demonstrable. As for the action of quinidine on the fibrillating auricle, it probably depends on the drug's depressor effect, if it is assumed that the fibrillation is due to excessive stimulation of the auricles by an absolutely or relatively increased resistance. C. L.

Ebeling, A. H., and **Fischer, A. Mixed cultures of pure strains of fibroblasts and epithelial cells.** *J. Exper. M.*, 1922, **36**, 285.

By growing epithelium and fibroblasts side by side in the same medium the authors found that they retained their individual characteristics, and when examined in section by van Gieson's stain the epithelium was coloured a greenish yellow while the fibroblasts and their fibrillae were pink. No transitional forms were observed between the two types of cells. There was thus no evidence of a 'dedifferentiation', the cells behaving according to the law 'omnis cellula e cellula eiusdem generis.' W. B.

Carrel, A., and **Ebeling, A. H. Pure cultures of large mononuclear leucocytes.** *J. Exper. M.*, 1922, **36**, 365.

The authors succeeded in growing large mononuclear leucocytes of the blood of the fowl for nearly three months *in vitro*. These 'large mononuclear leucocytes' corresponded to endothelial leucocytes, monocytes of Naegeli, blood histiocytes of Aschoff and Kiyono, or the haemo-macrophages of Metchnikoff, and when cultivated grew at a slower rate than fibroblasts. They had no tendency to form a tissue and were much less resistant than fibroblasts. Differentiation into cells assuming the appearance of fibroblasts took place under certain conditions. The activity of the large mononuclear cells was increased by contact with embryonic tissue juice, and inhibited by homologous serum. W. B.

Fischer, A. A pure strain of cartilage cells *in vitro*. *J. Exper. M.*, 1922, **36**, 379.

A strain of cartilage cells was obtained from the pars cartilago sclerae of the eye of chick embryos, and grown on a mixture of equal volumes of adult chicken plasma and juice from chick embryos. The initial growth of the cartilage cells was only possible on the free surface of the coagulum. In the course of growth the hyaline intercellular substance disappeared and the cells were spindle-shaped, growing in close contact and forming thin membranes. The rate of growth of cartilage was found to be slower than that of fibroblasts or epithelium. W. B.

Carrel, A. Growth-promoting function of leucocytes. *J. Exper. M.*, 1922, **36**, 385.

Carrel studied the growth-promoting effect of leucocytic extracts which were obtained from the blood of chickens by centrifugalization and extraction in Ringer's solution, the activity of such extracts being tested against fragments of chicken embryo heart and pure cultures of chicken fibroblasts. Leucocytic extracts were found to possess the power of increasing the rate of multiplication of fibroblasts *in vitro* and apparently they secrete substances *in vitro* which act in a similar way. Peritoneal exudate or connective tissue invaded by leucocytes acquires the power of increasing the rate of division of fibroblasts. Leucocytes are capable of bringing growth-activating substances to tissue cells, and may have an important function in promoting cell-multiplication in the parts of the organism where they accumulate. W. B.

Fischer, A. Cultures of organized tissues. *J. Exper. M.*, 1922, **36**, 393.

A fragment of small intestine was removed aseptically from chick embryos about 21 days old, and it was placed in a culture medium consisting of equal volumes of chick plasma and tissue juice. After a month's cultivation the tissues were fixed in formol-Ringer solution, and when sectioned it was found that the cylindrical epithelium had grown all round the fragment. The villi had disappeared and the connective tissue cells had formed a stroma with numerous fibrillae. There were no evidences of uncontrolled growth and no intermixing of the different cells. When the intestinal masses—'organisms' the author calls them—were cultivated in embryo juice without plasma the villi remained normal while the stroma progressively disappeared leaving an epithelial cyst. W. B.

Harris, W. H., and Friedrichs, A. V. (1). Periarteritis nodosa with a classification of the pathology. *J. Med. Research*, 1922, **43**, 285.

Harris, W. W., and Friedrichs, A. V. (2). The experimental production of periarteritis nodosa in the rabbit, with a consideration of the specific causal excitant. *J. Exper. M.*, 1922, **36**, 219.

In the first of these papers the authors give an account of a case of periarteritis nodosa occurring in a negro 32 years of age and classify the lesions into three groups. The primary lesion occurs in the arterial wall and is characterized by exudative and degenerative processes in the periadventitial structures, the adventitia, the media, and occasionally the intima. Acute, subacute and chronic inflammatory elements may be present. The second group of changes is consequent upon the severe wall injury as manifested by aneurysms both true and false, and haemorrhage extravasations. There are also proliferative and reparative processes and organization of the thrombi. The third group of changes includes the retrograde alterations in the organs following ischaemia and thrombosis. As the name periarteritis nodosa does not in general conform to the lesions found, the authors suggest the name 'periarteritis nodosa aneurysma thrombotica'.

In the second paper the authors report the results they obtained in attempts to transmit the disease to animals. The source of the material was the above mentioned case. The post-mortem was made 72 hours after death, the body being meantime kept in the refrigerator. Several nodules were excised from the kidneys and were found to give no growths on ordinary culture media. Nevertheless, when injected into rabbits, lesions were produced similar or identical with those met with in man. From one rabbit material was obtained and a suspension made from the liver, spleen, and kidney, and having been passed through a Berkefeld filter the filtrate was injected intravenously into a rabbit, which died in 3 months with typical lesions of periarteritis nodosa. The authors therefore claim that the virus is a filter-passer. The paper is illustrated by nine plates of microphotographs. W. B.

Harbitz, F. Unknown forms of arteritis, with special reference to their relation to syphilitic arteritis and periarteritis nodosa. *Am. J. M. Sc.*, 1922, **143**, 250.

Among certain cases of rare or unknown forms of arteritis the author describes a typical case of periarteritis nodosa occurring in a man 22 years of age and fatal in about ten months. The smaller arteries of the heart, the kidneys, stomach, intestine, the omentum, certain muscles and nerves, were the seat of typical lesions consisting of productive inflammation particularly in the media and intima. In the arteries of the muscles and nerves there was also an exudative process, particularly in the tunica adventitia. Microscopically, the appearances of the lesions suggested an infective character to the author, who considers that probably periarteritis nodosa is a definite disease due to a specific virus. W. B.

Boots, R. H., and Cullen, G. E. The hydrogen-ion concentration of joint exudates in rheumatic fever and other forms of arthritis. *J. Exper. M.*, 1922, **36**, 405.

The authors determined the hydrogen-ion concentration of joint exudates aspirated from patients with rheumatic fever, arthritis of undetermined cause and bacterial forms of arthritis. In the case of joint exudates from acute rheumatism the P_H was found to vary from 7·27 to 7·42. An exudate aspirated from a knee infected with *S. aureus* had P_H of 6·69 while an exudate from an infection with *Streptococcus haemolyticus* was also acid with a P_H of 6·19. The author infers from these figures that no free salicylic acid could possibly exist in such joint fluids following the administration of salicylates although this view has been expressed to account for the action of the drug. W. B.

BACTERIOLOGY

Brown, A. Studies in specific hypersensitiveness. 1. The diagnostic cutaneous reaction in allergy. Comparison of the intradermal method (Cooke) and the scratch method (Schloss). *J. Immunol.*, 1922, **7**, 97.

Van der Veer, A. 2. A comparison of various pollen extracts with reference to the question of their therapeutic value in hay fever. *Ibid.*, 1922, **7**, 113.

Cooke, R. A. (1). **3. On constitutional reactions: the dangers of the diagnostic cutaneous test and therapeutic injection of allergens.** *Ibid.*, 1922, **7**, 119.

Cooke, R. A. (2). **4. New etiologic factors in bronchial asthma.** *Ibid.*, 1922, **7**, 147.

Coca, A. F. 5. The preparation of fluid extracts and solutions for use in the diagnosis and treatment of the allergies, with notes on the collection of pollens. *Ibid.*, 1922, **7**, 163.

Spain, W. C. 6. Dermatitis venenata. *Ibid.*, 1922, **7**, 179.

Coca, A. F. 7. The age incidence of serum disease and of dermatitis venenata as compared with that of the natural allergies. *Ibid.*, 1922, **7**, 193.

Coca, A. F., Deibert, O., and **Menger, E. F. 8. On the relative susceptibility of the American Indian race and the white race to the allergies and to serum disease.** *Ibid.*, 1922, **7**, 201.

Cooke, R. A. 9. On the phenomenon of hyposensitization (the clinically lessened sensitiveness of allergy). *Ibid.*, 1922, **7**, 219.

This series of studies has been carried out in connexion with the Clinic of Applied Immunology at the New York Hospital. In the first paper the author has tested the relative value of the cutaneous or scratch method and the intradermal method in allergic conditions. The test proteins were employed either in the form of dry powders or fluid preparations. In a series of 78 comparative tests, the superiority of the intradermal over the scratch method was shown on the following grounds. (1) In every case known to be clinically sensitive to a protein, the intradermic test was positive, the scratch test with dry protein reacting in only half of the cases. Fluid preparations of proteins reacted negatively in 18 per cent. of the cases. (2) When properly applied the intradermic test is not so painful as the scratch method, and it takes less time to read the results.

In the second paper comparative tests were made with five products, four of which were purchased in the open market and one prepared by the author. A plea is entered for the use of larger doses and more potent agents than are usually employed.

In the third paper Cook gives a detailed account of the constitutional or general reactions in allergic patients based on an analysis of 578 cases examined and treated in 1920. Of these, 61 reacted constitutionally. Of the more usual symptoms seen, coryza, asthma, urticaria, erythema, pruritus, oedema, and cough were the most marked. Glandular enlargement, fever, nausea, diarrhoea, acute abdominal pain, dysmenorrhoea, cardiac collapse, were rare. The general symptoms may be immediate (within an hour) or delayed, and depend upon the mode of introduction of the allergen, the reactivity of the patient, the activity of the allergen employed, and particularly upon the concentration of the allergen and the total amount given. Cumulative results may occur with one and the same allergen, but also when different allergens are used. Constitutional symptoms were seen after the injection of very many kinds of allergens derived from plants or animals. With regard to the treatment of constitutional symptoms the author recommends that on the first manifestations a tourniquet should be tightly applied to the arm above the site of the injections to prevent the transport of more allergen to hypersensitive tissues by the blood or lymphatic routes. Adrenalin should also be freely given.

In the fourth paper the author deals with certain new aetiological factors in bronchial asthma and concludes that the group of substances absorbed by inhalation plays a much more important part in causing asthma than has generally been believed. Coca, in the fifth paper, deals with the preparation of fluid extracts and solutions for the diagnosis and treatment of the allergic states, details being given of the preparation of extracts from wheat, rice, beans, horse dandruff, pollen, and other substances. Spain deals with the allergic phenomena following exposure to the poison ivy (*Toxicodendron radicans*). As is well known this plant causes, in certain persons, erythema, hyperaemic macules, papules, vesicles, and pustules with extreme itching and a burning, stinging heat. The exact nature of the intoxication is not understood. Spain produced the typical vesicular lesions by means of an alcoholic or chloroform extract of the fresh leaves of the plant applied to the surface of the skin. Intradermal injection of an active alcoholic extract did not produce vesicles. Varying degrees of susceptibility were demonstrated in different persons.

In the seventh paper of the series Coca deals with the age incidence of serum disease and of dermatitis venenata in comparison with that of the natural allergic reactions. Serum disease differs from other forms of human hypersensitiveness in the almost constant characteristic of the incubation period and its high percentage incidence. Dermatitis venenata differs from other types of hypersensitiveness in the constant and characteristic nature of the lesion. The age incidence of the ‘natural’ allergies increases rapidly in the early age periods, but probably does not greatly exceed 10 per cent. in any period. The age incidence of dermatitis venenata increases greatly from childhood to adult life and reaches a high percentage (*circa* 90 per cent.). The age incidence of serum disease seems unchangeable. Thus the percentage incidence of serum disease at the age periods 0–5 years, 6–10, 11–15, 16–25, and 25 years upwards was found to be 10·2, 12·5, 11·6, 13·8, and 10·4 per cent. respectively.

In the eighth paper Coca, Deibert, and Menger deal with the relative susceptibility of the American Indian races and the white race to the allergies and to serum disease. Inquiries indicated that the allergic trait is much less marked among the American Indians than in the white race, and actual experiments were made on 26 volunteer full-blooded Indians, all students of the Haskell Institute, in Lawrence, Kansas. The material injected was fresh normal horse-serum preserved with cresol, the dose being mostly 110 c.cm. 46 per cent. of those injected became affected with rashes, and joint pains with or without fever. This percentage is much lower than that obtained by Longcope and by Cole, who made their observations on white people. In the last paper, Cooke deals with the quantitative relations in partial desensitization as contrasted with those that obtain in the state of lessened sensitiveness in allergy. He considers that there is a difference in the mechanism of these two phenomena, and he proposes to call the latter hyposensitization. W. B.

Weichardt, W. (editor). Ergebnisse der Hygiene, Bakteriologie, Immunitätsforschung und experimentellen Therapie. [**Results of researches in hygiene, bacteriology, immunity, and experimental therapy.**] *Berlin*, 1922 (*J. Springer*), p. 902.

In the fifth volume of Weichardt's 'Ergebnisse', a serious attempt is made to deal with the vast accumulations of literature on subjects of surpassing interest to bacteriologists, hygienists, and serologists. Thus R. Pfeiffer considers the influenza problem as a whole, while Hübschmann has made a further analysis of over 400 papers on influenza. Of peculiar interest is the exhaustive, clearly-expressed article of Doerr, which deals in 200 pages with the anaphylaxis literature from 1914–21. Nearly 600 papers are analysed in a critical and masterly manner, which will prove of great service to workers in this field. The editor, Weichardt, writes on the basis of protein-therapy, a subject also dealt with by M. Claus. The ever-growing literature on encephalitis lethargica is treated by Gottstein, the recent developments in the sero-diagnosis of syphilis by Baumgärtel, the theory and technique of the Weil-Felix reaction by G. Wolff, the most recent researches on anthrax by K. Poppe, *Bacillus proteus* by H. Zeiss, war epidemics by Solbrig, and social hygienic problems by Dresel. W. B.

Hall, I. W. Indicators for culture media containing varying acids and buffers. *Brit. J. Exper. Path.*, 1922, **3**, 182.

Brom-phenol blue, methyl red, and phenol red may be used as P_H indicators for bacteriological media containing dilute quantities of certain typical mineral and organic acids. Buffer indices of media are slightly altered when small amounts of blood or of dilute acids are added. They are unaffected by storage. P. F.

Kodama, H. Ein neuer elektiver Nährboden für Choleravibrionen. [**A new selective medium for cholera vibrios.**] *Centralbl. f. Bakteriol.* (&c.), Abt. 1, 1922, Orig. **88**, 433.

The new medium is designed to reveal the diastatic action of *V. cholerae* on starch. A mixture is made of 100 c.cm. 3 per cent. neutral litmus agar, 1 c.cm. 10 per cent. soda solution, 0·5 c.cm. sat. alcoholic solution of fuchsin, 2·5 c.cm. freshly-prepared 10 per cent. sodium sulphite solution, and 3 gm. of finely suspended potato starch in 5 c.cm. of water. The mixture is steamed for half an hour. A second mixture is made consisting of 100 c.cm. of water containing 20 parts of ox serum and 1 c.cm. of 10 per cent. sodium hydrate solution. This is likewise steamed for half an hour. Two parts of the first mixture are added to one part of the second, and sterilization is effected discontinuously in the usual way. On the surface of this medium the cholera vibrio grow at first white, but in 3 to 9 hours the colonies become an intense red and two types are seen: (1) flat colonies, 0·3 to 0·7 cm. in diameter, not raised and with irregular edges; (2) sharp-edged, raised colonies measuring 0·1 to 0·2 cm. A clear halo is seen surrounding both types of colonies. Merck's soluble starch was also found to be effective in replacing potato starch. Dextrin media showed only raised, round colonies without a halo. W. B.

Kodama, H., u. Takeda, H. Eine neue biologische Reaktion der Choleravibrionen. [**A new biological reaction for *V. cholerae.***] *Centralbl. f. Bakteriol.* (&c.), Abt. 1, 1922, Orig. **88**, 513.

The authors draw attention to the production of a diastatic ferment by *V. cholerae.* They used a medium which contained Witte peptone 1 gm., potato starch 0·5 gm., and 2 c.cm. of 10 per cent. soda solution, the change in the starch being estimated by testing with Lugol's solution. They find the diastatic action most strongly marked in the case of *V. cholerae*, less so with the vibrios of Finkler and Prior, and of Metchnikoff, and very slight in the case of *B. anthracis*, *B. subtilis*, and *B. coli.* They assert that when stools are cultivated in the above medium, and when the subsequent addition of Lugol's solution produces no change in colour, the existence of cholera is suggested. W. B.

Hartley, P., and Hartley, Olga. The routine preparation of diphtheria toxin. *J. Path. & Bacteriol.*, 1922, **25**, 458.

The authors deal in detail with the methods they have elaborated for the production of diphtheria toxin. These details must be consulted in the original, and it must suffice here to state that among the factors governing the production of toxin they emphasize in particular the strain of the bacillus, the nature and quality of the peptone, the initial reaction of the medium, the temperature of sterilization, and the volume of broth inoculated. Even in spite of the most careful attention to every detail there still remain vagaries in the strength of the toxin, which are difficult to forsee or to understand. W. B.

Abt, G., et Loiseau, G. Réaction du milieu et production de la toxine diphtérique. [**Reaction of media and the production of diphtheria toxin.**] *Ann. de l'Inst. Pasteur*, 1922, **36**, 535.

From an elaborate experimental study the authors conclude that the first essential for the manufacture of potent diphtheria toxin is that the medium shall be good. The medium of L. Martin adjusted to a P_H of 7·5 to 7·9 gives very regular results and yields high-grade toxin. W. B.

Ayres, S. H., and Mudge, C. S. The relation of vitamins to the growth of a streptococcus. *J. Bact.*, 1922, **7**, 449.

The authors have studied the effect of water-soluble vitamin B and the fat-soluble vitamin A on the growth of a pathogenic streptococcus. They found that autolysed yeast extract contained growth-promoting substances; the water-soluble B did not, however, appear to be one of them. Cabbage extract also promoted growth, but a glucose solution containing the same amount of sugar had a similar effect. Fats and oils, vegetable, animal, and mineral, even in very small amounts, were found to stimulate the growth of the streptococcus studied. W. B.

Sonne, C. Investigations on guinea-pigs relating to the influence of the light bath on the action of diphtheria toxin in the organism. *Acta Med. Scand.*, 1922, **56**, 619.

Sonne's investigations were instigated by the work of Famulener and Thorvald Madsen in 1908 ('Die Abschwächung der Antigene durch Erwärmung,' *Biochem. Ztschr.*, **11**, 186). He found that by applying visible rays to the surface of the skin, the temperature of the blood in and below the skin can be raised to 47°–48° C., and that if the duration of the light bath be one of 2 hours, it is probable that all the blood in the body has been heated to this temperature for about 15 minutes. The two following experiments show that the toxin of diphtheria is destroyed to a considerable extent by heating to 48° C. A solution of toxin (1:200) in a test-tube was heated in a water-bath at 48° C. for an hour. Two guinea-pigs, weighing 230 and 270 gm. respectively, were each given subcutaneous injections of 1 c.cm. Only a very slight infiltration followed, and the animals continued constantly to gain weight. Two other guinea-pigs were given injections of the same quantity of unheated toxin, and both showed severe infiltration at the site of injection, and lost weight appreciably. Thirty-eight guinea-pigs were given subcutaneous injections of a minimum lethal dose of toxin, and nineteen were also given a single light bath of 2 hours' duration immediately after the injection, the source of the light being a large carbon arc lamp of about 50 ampères. To eliminate the ultra-red and ultra-violet rays, the light was filtered through a Finsen sun lens. As the tabulated results show, the animals treated with light were considerably more resistant to the toxin than the others, and the conclusion to which Sonne comes is that at least 40 per cent. of the injected toxin was destroyed by the light bath. The specific heating of the blood was probably the main factor in these results. C. L.

Brown, J. H., and **Howe, P. E. Transparent milk as a bacteriological medium.** *J. Bact.*, 1922, **7**, 511.

The authors describe the use of transparent milk as a culture medium. One part of skim milk is mixed with two parts of water and 0·4 per cent. of sodium citrate. After standing about an hour the clarified milk may be filtered. To avoid caramelization of the lactose during sterilization the reaction is adjusted to about P_H 6·8. During each steaming a heavy precipitate is thrown down but redissolves on cooling. W. B.

Tsukahara, I. Untersuchungen über das Vorkommen von Diphtheriebazillen in der Scheide von Gebärenden und Wöchnerinnen sowie bei Neugeborenen. [**The occurrence of diphtheria bacilli in the vagina of pregnant and puerperal women and in the newly born.**] *Centralbl. f. Bakteriol.* (&c.), Abt. 1, 1922, **88**, 366.

During the last decade a considerable literature has accumulated on the occurrence of diphtheria and diphtheria bacilli in the newly born, especially in lying-in institutions, foundling hospitals, and homes for children. While some have attributed little significance to the mere occurrence of *B. diphtheriae* in the newly born, others have considered that it possesses considerable powers of setting up various morbid states. In a large number of cases the bacilli have been reported as occurring in the nose, and it has been supposed that the infection may come from the genital organs of the mother, especially as diphtheria bacilli have been stated to occur there. The present author made a careful examination of the bacteria in the maternal vulva and vagina and of the nose of the child in 60 individual cases and never found the true diphtheria bacillus. Eleven times, however, he found diphtheroids distinguishable from Loeffler's bacilli on biochemical tests and he considers that errors in diagnosis have occurred from the neglect of such tests. He considers that diphtheria in the newly born is a post-natal infection. W. B.

Cowan, Mary L. Variation phenomena in streptococci, with special reference to colony form, haemolysin-production, and virulence. *Brit. J. Exper. Path.*, 1922, **3**, 187.

Individual strains of streptococci can be 'dissociated' into 'rough' and 'smooth' types which show remarkable differences in virulence for laboratory animals. Inoculation with the 'rough' or avirulent type appears to afford considerable protection against the 'smooth' or highly virulent form. Haemolysin production is not a dominating factor in streptococci virulence. P. F.

Schumacher, J. Welche chemische Substanz baut die Polkörnchen des Diphtheriebazillus auf? [**Of what chemical substance are the polar bodies of the diphtheria bacillus composed?**] *Centralbl. f. Bakteriol.* (&c.), Abt. 1, 1922, **88**, 362.

From the results of micro-chemical investigations, the author believes that the Babes-Ernst granules in the diphtheria bacillus are composed of free diphtheria nucleic acid. When films are stained with carbol-methylene blue and are subsequently treated with a 1 per cent. watery phosphin solution (chrysanilin extra Kahlbaum) the polar bodies are green and the bacilli stain yellow. With a ½ per cent. solution of ruthenium chloride, the polar bodies are of a grey-black colour, the bacillary bodies being a pale grey. With carbol-methylene blue and subsequent treatment with 1 per cent. solution of quinine hydrochloride and eosin the granules stain blue while the bacillary bodies are pink. W. B.

Stangl, F. H. The local inflammatory reaction produced by the tetanus bacillus. *J. Infect. Dis.*, 1922, **31**, 22.

The author has studied the pathology of the local reaction following the subcutaneous and intramuscular injection of pure cultures of *B. tetani* into guinea-pigs. Serial sections were made of the lesions from 12 hours onwards. An intense cellular infiltration was found in the area of inoculation, wandering and fixed cells both taking part in its production. In the early stage from 80 to 90 per cent. of the cells are polymorphonuclear. The tetanus bacilli occur chiefly in clumps scattered in the spaces between the leucocytes and the fixed cells. A few bacilli may be taken up by the leucocytes. In the older lesions the polymorphs are replaced by mononuclear types. The muscle-cells degenerate and giant cells make their appearance. In one human case examined the local reaction to tetanus bacillus corresponded in essentials to the reaction in the guinea-pig. W. B.

TENBROECK, C., and BAUER, J. H. The tetanus bacillus as an intestinal saprophyte in man. *J. Exper. M.*, 1922, **36**, 261.

It is generally stated that the tetanus bacillus is present in the faeces of man, but little accurate work has been done on the subject. In 100 specimens Pizzini (1898) found it in 5 per cent. of the cases he examined, whereas Tulloch (1919–20), in 21 men returned from overseas service, was successful in no less than 7 cases (33 per cent.). From the faeces of 31 civilians in England he obtained tetanus bacilli 5 times (16 per cent.). The present authors examined the faeces of 78 individuals, all, with one exception, being male Chinese from 5 to 44 years of age. Tetanus bacilli were found in 34·7 per cent. There was some evidence that the tetanus bacilli multiplied in the alimentary canal, as bacilli were being excreted by individuals living on a practically sterile diet for a month or more. Suspensions of the stools were heated to 80° C. for 20 minutes and were then transferred to sugar-free bouillon containing a piece of kidney in a fermentation-tube. After 4 days, attempts were made to isolate pure cultures, and when successful the toxic effect on mice and the neutralizing effect of tetanus antitoxin was determined. W. B.

REDDISH, G. F., and RETTGER, L. F. *Clostridium butyricum* (*B. putrificus*, Bienstock), a distinct species. *J. Bact.*, 1922, **7**, 505.

There has always been a good deal of doubt as to the species rank of *B. putrificus*, Bienstock, 1899. From their experience the Anaerobic Committee of the M.R.C. believed that '*B. putrificus*' was frequently at any rate a mixture of *B. cochlearius* or *B. tertius* with *B. sporogenes*. The present authors regard this view to be incorrect and consider that *B. putrificus* is a species with round terminal spores. [It may be said, however, that in the photographs accompanying Bienstock's (1899) paper spores are figured both round and oval, the latter greatly predominating—*Reviewer*.] Reddish and Rettger describe *B. putrificus* as resembling *B. tetani* and *B. tetanoides*, but differing in being proteolytic and non-saccharolytic, or but feebly so, and they consider there are sufficient morphological, cultural, and biochemical characters to separate Bienstock's anaerobe from others. W. B.

MAITLAND, H. B. Experiments employing a quantitative method in a study of the d'Hérelle phenomenon. *Brit. J. Exper. Path.*, 1922, **3**, 173.

A quantitative method for estimating the strength of a sample of the active principle which causes the d'Hérelle phenomenon is described. Employing this method, the rate of increase of active principle in a bouillon culture was determined. There was an early period of lag, a short period of rapid increase, and an indefinitely prolonged period of equilibrium. The increase of the active principle did not coincide with any constant alteration in the total bacterial content of the culture in which it was increasing. Lysis did not always occur; sometimes there was an increase in the total number of bacteria. Increase was shown to require three factors—active principle, living bacteria, and some additional factor. Several substances were found to contain this factor: for instance, nutrient broth, meat infusion, ascitic fluid, human plasma, or potato. Haemoglobin was without effect.

P. F.

Fleming, A., and **Allison, V. D.** **Observations on a bacteriolytic substance ('lysozyme') found in secretions and tissues.** *Brit. J. Exper. Path.*, 1922, **3**, 252.

There exists in human secretions and tissues (with few exceptions), as well as in animal and some vegetable tissues, a powerful bacteriolytic agent, 'lysozyme'. The lytic action of this substance is especially manifested on certain non-pathogenic bacteria, and in all probability it is the cause of such bacteria being non-pathogenic: but it is exerted also on some bacteria which are pathogenic to the lower animals and some which have been isolated from the human body. A large non-pathogenic coccus has been used as an indicator microbe in the investigation of the distribution of lysozyme. It has been found that the lytic substance is present in secretions, especially in tears, nasal mucus, and sputum, and in tissues, especially in cartilage, while it is present in large quantity in white of egg. The properties of lysozyme are detailed. Resistant forms of the indicator coccus are readily developed, and it is found that strains made resistant to one tissue are equally resistant to all tissues, indicating the essential similarity of lysozyme from different sources. Lysozyme is not absorbed by saturation with the test microbe, but, on the other hand, the lytic power is increased, and the increase is dependent on the number of microbes dissolved. It has not been found possible to transmit the lytic principle in series, as can be done with the 'bacteriophage', and a consideration of the properties of lysozyme and the bacteriophage makes it clear that there are fundamental differences between them. (*vide* Fleming, *Medical Science*, 1922, **7**, 255). P. F.

Doerr, R. Die Bakteriophagen. (Phänomen von Twort und d'Hérelle.) [**Bacteriophages. (Phenomenon of Twort and d'Hérelle.)**] *Klin. Wchnschr.*, 1922, **1**, 1489, 1537.

This is a clear and critical exposition of the Twort-d'Hérelle phenomenon and deals with the most recent work on the subject. W. B.

Prausnitz, C. Über die Natur des d'Hérelle'schen Phänomens. [**On the nature of the d'Hérelle phenomenon.**] *Klin. Wchnschr.*, 1922, **1**, 1639.

From his experiments the author is inclined to the belief that 'bacteriophage' is an ultravisible virus—as maintained by d'Hérelle. He finds that it consists of particles which are of the order of 20 $\mu\mu$, i. e. much larger than those of pepsin, typsin, and invertase. The 'bacteriophage' is destroyed by certain chemicals of the naphthalin series, especially tetralin, while the abovementioned enzymes are resistant. Antibacteriophagic serum, obtained by injecting rabbits with bacteriophagic substance, when exhausted with the homologous bacilli is robbed only of its antibacterial properties, its antibacteriophagic properties remaining. From an incompletely neutralized bacteriophagic-antibacteriophagic mixture the author grew a bacteriophagic strain which was completely serum-fast. W. B.

Davison, W. C. **Observations on the properties of bacteriolysants (d'Hérelle's phenomenon, bacteriophage, bacteriolytic agent, &c.).** *J. Bact.*, 1922, **7**, 475; 491.

The author finds that filtrates of the stools of infants suffering from bacillary dysentery, acute intestinal indigestion, and otitis media were bacteriolytic for one or more of 27 strains of Flexner, Shiga, or typhoid bacilli. He considers that the d'Hérelle phenomenon is non-specific, and that a bacteriolysant from the stool of a patient may not be so active against homologous as against heterologous strains. He does not consider that it plays a part in immunity as an active bacteriolysant was obtained from a patient the day before his death. The bacteriolytic activity of a bacteriolysant may or may not be exalted by passage through living cultures of dysentery bacilli, but it is attenuated by passage through sterile peptone water and dead dysentery bacilli. Heating to 60 to 70° C. for 45 to 60 minutes had little or no effect upon the activity of a filtrate. Bacteriolysants produce lysis more completely in low dilutions and at a P_H of 8·0 and 8·2. Bacteriolysants were non-pathogenic for a rabbit. 'Moth-eaten' or sensitive colonies were obtained in subcultures of dysentery bacilli which had been attacked by a bacteriolysant. They were subcultured for 42 generations. The media in which they were grown, the solutions in which they were washed, and the suspensions of disintegrated 'sensitive' bacilli were all strongly bacteriolytic. The author thinks it possible that the lytic principle in d'Hérelle's phenomenon is an enzyme, but it is not trypsin. This lytic enzyme not only dissolves bacteria but also favours the multiplication of bacteria which produce the enzyme. In this way the author supposes that the bacteriolytic enzyme is carried from generation to generation.

W. B.

KLIGLER, I. J. The cultivation of *Spironema duttoni* from a case of relapsing fever. *Brit. J. Exper. Path.*, 1922, **3**, 215.

A case is reported which was apparently an atypical case of Palestinian relapsing fever. The spirochaetes were so few in number that they were missed during the first attack even in the thick drop, and only a scattered few found during the second and third attacks. At the time of the third attack successful blood-cultures were made by a special method. These were kept over a month and passed to the third generation, when they were lost by a mould contamination. Transplants were made after 16 and 18 days respectively. Successful rat inoculations were also made and the strain carried through three rat passages. The character of the culture and the course of the rat infection are described. The special method referred to consists in the addition of peptone to horse or rabbit serum or ascitic fluid in order to stabilize the reaction. A fibrin 'basket' is also obtained by the addition of a small quantity of fresh blood and strict anaerobic conditions instituted.

P. F.

CLAUSEN, S. W., and **JEANS, P. C. The distribution and secretion of arsenic after intravenous administration of arsphenamine in children.** *Am. J. Syph.*, 1922, **6**, 556–67.

Clausen and Jeans have studied the distribution and excretion of arsenic after intravenous injection of arsphenamine in children. They found that arsphenamine rapidly disappeared from the blood, but 10 per cent. remained for one hour. The largest amounts of the drug were taken up by the liver and intestines. Excretion began immediately, was rapid at first, but gradually diminished for two weeks, when only traces were found. But after two or three weeks 50 per cent. was still present in the tissues. It was excreted five times as rapidly in the faeces as in the urine. Arsenic was found in the cerebrospinal fluid (after intravenous injection), the amount depending on the degree of inflammation present. The greatest quantity was found in cases with evidence of active neurosyphilis, more in infants than older children; while in some cases with no evidence of neurosyphilis arsenic was absent. The authors conclude that the amount of arsenic in the cerebrospinal fluid is as great after intravenous injection as after intraspinal injection of arsphenamine serum by the Swift-Ellis method, in cerebrospinal syphilis.

C. F. M.

Lee, D. C. A contribution to the action of arsphenamine and mercury on the *Treponema pallidum*. *Am. J. Syph.*, 1922, **6**, 546–50.

Lee has experimented on the action of arsphenamine and mercury on the *Spironema pallidum in vitro*. He found that the spirochaetes were not killed by arsphenamine and neoarsphenamine in dilutions of 1 in 130, and silversalvarsan in dilutions of 1 in 125, or by salvarsanized serum from blood drawn at 2-hour intervals for 12 to 48 hours after injection. Salvarsanized tissue extract, 24 hours after injection, however, killed the spirochaetes in 6 to 12 hours. He concludes that salvarsan acts on the spirochaetes by combining with the cellular protein, producing an arseno-protein which is detrimental to the parasite and makes it an easy prey to the protective powers of the body. Mercury preparations, on the other hand, are direct chemical poisons to the spirochaete. Bichloride of mercury, 1 in 1,000, killed them in 6–8 hours, and benzoate of mercury, 1 in 450, in 12–24 hours.

C. F. M.

Pearce, L., and Brown, W. H. A study of the relation of *Treponema pallidum* to lymphoid tissue in experimental syphilis. *J. Exper. Med.*, 1922, **35**, 39–62.

Pearce and Brown find that a widespread dissemination of *Spironema pallidum* in rabbits after inoculation takes place by way of the lymphatics, and that syphilis in the rabbit is primarily an infection of lymphoid tissue. This dissemination takes place within 48 hours, and *S. pallidum* is present in the regional lymphatic glands as early as two days after inoculation. It is also found in the popliteal and other glands. Orchitis resulting from injection into the testicle of an emulsion of infected lymph-glands is of a rapidly progressive type. Active spironemata survive in the lymph-glands for long periods of time and can be found in them in latent cases with no symptoms. The lymph-glands, therefore, act as reservoirs for the spironemata.

C. F. M.

Fildes, P. The nature of the action of potato upon the growth of *B. influenzae*. *Brit. J. Exper. Path.*, 1922, **3**, 210.

It is suggested that the stimulating action of potato upon the growth of *B. influenzae* is due to the action of the peroxidase enzyme operating in the same manner as blood-pigment to accelerate the transfer of atmospheric oxygen to the bacillus. (Vide Fildes, *Medical Science*, 1921, **4**, 156. Thjötta and Avery, *Medical Science*, 1922, **6**, 62).

P. F.

Jones, F. S. The source of the micro-organisms in the lungs of normal animals. *J. Exper. M.*, 1922, **36**, 317.

The author examined the bacterial content of the lungs of calves, rabbits, guinea-pigs, rats, and white mice that had been killed immediately before. The principal microbes found were streptothrix (87 times), *B. subtilis* (41), moulds (25). These forms probably originated in dry foodstuffs such as hay. By withholding or moistening such food it was found that the number of microbes in the lungs diminished. The bronchial glands of guinea-pigs showed infection of 66·6 per cent. of the tubes of media inoculated.

W. B.

Strauss, W. Versuche über beim Sprechen verschleuderte Tröpfchen. [**On the scattering of droplets in the act of speaking.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1922, **96**, 27.

By means of exposed microscopic slides and culture media the author has made a study of the scattering of micro-organisms from the mouth during the act of speaking. In general the dissemination was not found to take place farther than about 30 cm., and it depended on a variety of factors, the more important of which were the loudness and continuity of the speech, the amount of saliva in the mouth, the existence of various anomalies of the mouth, teeth, and larynx, and whether consonants or vowels were pronounced. Experiments were also made on patients suffering from various conditions such as ulcerative stomatitis, pyorrhoea alveolaris, and diphtheria in either the acute or carrier stage. The risk of dissemination during speaking was found to be less than is generally supposed. Out of 8 diphtheria cases with marked tonsillar infection only 2 showed diphtheria bacilli in mouth droplets produced during loud speaking. In acute catarrhal conditions, however, many infected droplets were expelled. Even during screaming in children the scattering of bacteria was slight. The danger of dissemination of the viruses of the exanthemata was believed to be great.

W. B.

Mackie, T. J. The serological relationships of the paracholera vibrios to *Vibrio cholerae*, and the serological races of the paracholera group. *Brit. J. Exper. Path.*, 1922, **3**, 231.

The paracholera vibrios comprise a group which is not serologically homogeneous, but, in addition to *V. paracholerae* A and B already described, represents a considerable number of serological races precisely differentiated by agglutination reactions. By direct agglutination tests, using plain saline emulsions and incubating at 37° C. for 2 hours, the paracholera vibrios are distinctly differentiated from *V. cholerae*. *V. cholerae* antiserum exhibits apparent coagglutination under certain conditions towards *V. paracholerae* A and certain similar types; this effect develops more slowly than the agglutination of the homologous organism and is of lesser degree and of lower end-titre; it is most markedly elicited when formol-broth emulsions are used and the tubes are incubated first at 55° C.

P. F.

Dudley, S. F. The relation of natural diphtheria anti-toxin in the blood of man to previous infection with diphtheria bacilli. *Brit. J. Exper. Path.*, 1922, **3**, 204.

The author had the opportunity to examine by Schick's method a school in which diphtheria was prevalent during a long period. He found that 'new' boys were three times as often susceptible to diphtheria as 'old' boys. A graph is shown which indicates that the 'old' boys became immune during outbreaks of diphtheria, and that between outbreaks no immunity was developed. The fact that the 'old' boys were older was insufficient to account for the more frequent immunity. In the course of three months 32 per cent. of the susceptible boys became immune. In the course of nine months 92 per cent. of the boys who developed clinical diphtheria became immune. The period of 'carrying' diphtheria bacilli was always short, and it is estimated that during seven months 30 per cent. of the boys were recognizable carriers. Under these circumstances it is probable that all boys in the school had the opportunity of being infected by the diphtheria bacillus to a slight, unrecognizable degree.

From these results it may be deduced that exposure to infection resulting in slight multiplication of diphtheria bacilli in the throat is the immediate cause of the 'natural' immunity to diphtheria which develops in many communities from the age of 18 months upwards. Incidentally, the author's work indicates that caution is necessary in attributing the development of immunity in a community to any inoculation with toxin-antitoxin mixtures which may have been carried out. P. F.

Cummins, S. L. Agglutination of washed red blood-corpuscles by colloidal silica. *Brit. J. Exper. Path.*, 1922, **3**, 260.

Colloidal silica solution to which sufficient salt has been added to bring the mixture up to 0·75 per cent. of NaCl brings about rapid agglutination of washed red blood corpuscles, and this result can still be obtained after considerable dilution. The flocculation and sedimentation of washed red cells by colloidal silica as above is to a great extent prevented by the presence of concentrated human serum, this inhibition disappearing as the serum is made more dilute. The inhibition seems to depend upon the formation of a gel. P. F.

Beaton, E. On the antitryptic action of the blood. *Brit. J. Exper. Path.*, 1922, **3**, 224.

The albumin-fraction of the serum-proteins is more antitryptic than the globulin fraction, and in human serum the inhibiting factor lies almost entirely in the former. This association of the antitryptic action with the albumin-fraction applies also to the abnormal increment of antitrypsin occurring in certain conditions of disease. There is no proportional relation between the antitryptic power of the serum and the concentration, either of the total protein or of the albumin; but, on the contrary, an increased inhibitory capacity may be accompanied by a diminished protein content, and especially by a diminished albumin content. The antitryptic power of the serum cannot be conceived as due to a simple diversion of the enzyme by the protein as such, but must be dependent upon some at present unrecognized character of this protein. P. F.

Wyard, S. Precipitins and the aetiology of serum sickness. *J. Path. & Bacteriol.*, 1922, **25**, 191.

The author has investigated the connexion between serum sickness and circulating precipitins in the blood of the patient and has found no relation between the two. Patients whose serum contains precipitins are in no way more likely to suffer from serum sickness than those in which no precipitins can be demonstrated. The antigenic properties of horse serum vary with the source of the serum. W. B.

Hektoen, L., and **Schulhof, K.** **On specific erythro precipitins (hemoglobin precipitins ?).** *J. Infect. Dis.*, 1922, **31**, 32.

This paper deals with experiments in precipitin formation in response to aqueous extracts of blood corpuscles. Rabbits were the animals employed, and the extracts were obtained from the ox, dog, pig, horse, and other animals, including man and monkeys. Precipitins were produced and were found to act on the constituents of the red corpuscles, in some cases only on the species (dog, horse, pig) furnishing the corpuscles, in other cases extending to the red corpuscles of other animals. Conversion of haemoglobin into carboxyhaemoglobin, sulphydrohaemoglobin or methaemoglobin was not found to affect the specific serum precipitation. On splitting haemoglobin into haematin and globin by acetic acid the precipitinogenic elements were found to remain in solution after removal of the globin, which did not appear to be responsible for the antigenic properties of the haemoglobin. Ordinarily, however, the precipitinogens are attached to the haemoglobin molecule and are not removed or diminished by repeated crystallization. W. B.

Hektoen, L. **The specific precipitin reaction of the normal and cataractous lens.** *J. Infect. Dis.*, 1922, **31**, 72.

Long ago, Uhlenhuth discovered that the lens of different animals contains identical antigenic elements. Thus a lens antiserum prepared by injecting rabbits or guinea-pigs with extracts of the lens of the ox reacts in precipitation, anaphylaxis, and fixation tests not only with the lens of the ox but also with the lens of other animals, including birds, amphibians, and even fish. The lens is said to be highly 'organ specific' and not 'species specific', as is so often the case. The present author has tested the precipitin reactions of the lens of man (human and cataractous), monkey, rabbit, rat, sheep, pig, ox, chicken, and dog, and has confirmed the organ specificity. The normal lens gives no evidence of a species-specificity. This is also true of the lens of human senile cataract except that 8 of 50 cataractous lenses gave a reaction with human serum albumin. In some cases it appeared that the foetal human lens contained species-specific elements. The lens-specific elements in normal, cataractous, and foetal lenses are probably not identical precipitinogenically. W. B.

Grass, H. Versuche zur Wildbolzschen Eigenharnreaktion. [**Experiments with Wildbolz's auto-urine test.**] *Beitr. z. Klin. d. Tuberk.*, 1922, **51**, 157.

Grass has investigated the Wildbolz auto-urine reaction in 145 cases of tuberculosis, and has found that no relationship could be established between the character of the reaction and the severity of the disease. He suggests that the reaction depends solely on the salts in the urine, i. e. that it is a chemical-traumatic phenomenon, independent of the antigen content of the urine. The technique recommended by Wildbolz for preparing the urine is, in the opinion of Grass, likely to destroy any antigens it may contain. C. L.

Kuhn, Hedwig. Beitrag zur Kenntnis der Eigenharnreaktion nach Professor Wildbolz. [**A contribution to the study of Prof. Wildbolz's auto-urine reaction.**] *Beitr. z. Klin. d. Tuberk.*, 1922, **51**, 24.

Hedwig Kuhn has experimented with the Wildbolz auto-urine reaction in 154 cases of tuberculosis, and in about a score of healthy persons. Although the reaction was much more often positive in cases of active than in cases of latent tuberculosis, the exceptions were numerous enough to raise serious doubts as to the test being specific. Probably it is specific, but at the present stage it is not to be relied on in distinguishing between active and latent tuberculosis. In 77 per cent. of all the cases the behaviour of the reaction was in conformity with the claims of its sponsors: in 11 per cent. its behaviour was doubtful, and in the remaining 12 per cent. misleading. In some cases the reaction was negative, even with highly-concentrated urine, and this observation negatives the teaching that a positive reaction depends only on the concentration of the urine. C. L.

Gottschalk, A. Die kurvenmässige Darstellung des Ausfalles der Urochromogenreaktion in ihrer Bedeutung für die Beurteilung der Form und Prognose der Lungenphthise. [**The graphic representation of the result of the urochromogen reaction with relation to forming an estimate of the character and prognosis of pulmonary tuberculosis.**] *Beitr. z. Klin. d. Tuberk.*, 1922, **51**, 1.

Using Moeller's modification of the urochromogen reaction, Gottschalk has found that it is a reliable guide to prognosis, and that its behaviour in one and the same case over a considerable period coincides with certain other phenomena such as changes in the weight and temperature. The reaction was almost invariably negative when the disease was stationary and unaccompanied by appreciable fever, and it was positive when rapidly progressive disease was accompanied by fever and loss of weight. When the character of the disease changed from latency to marked activity, a negative urochromogen reaction became more and more positive. Its prognostic significance is, therefore, considerable. C. L.

Rogers, J. B. The effect of sunlight and oven heat on experimental tuberculosis. *Am. Rev. Tuberc.*, 1922, **6**, 119–26.

Ninety guinea-pigs were infected with virulent human tubercle bacilli, either by inhalation or subcutaneous inoculation. Then 34 were exposed daily to natural sunlight, the duration of the exposures being gradually increased from 5 minutes to several hours a day during an average period of 51 days. The average duration of life was 47 days. 27 guinea-pigs were exposed to dry heat at a temperature ranging from 55° to 65° C. for 5 minutes, 20 of them 24 hours after inoculation, and 7 of them 3 days after. Their average duration of life was 48 days. The average duration of life of the 29 'control' guinea-pigs was 48½ days. The tuberculous involvement was approximately the same in all 3 classes. The experiment with dry heat was repeated with 16 mice given intraperitoneal injections of virulent bovine tubercle bacilli. The heated and non-heated mice showed approximately the same amount of tuberculous involvement. C. L.

Cooke, J. V. The transmission of complement-fixing substances from mother to child. [**B.**] *Am. Rev. Tuberc.*, 1922, **6**, 127–33.

The examination by Rosencrantz for complement-fixing substances in the umbilical blood of infants at birth has been repeated by Cooke, who used a whole bacterial emulsion antigen and inactivated serum. In several cases the blood of the mother and of the infant was examined some time after birth by the complement-fixation test. Complement-fixing antibodies were shown to have been transmitted from the maternal blood to the offspring in whom they persisted for a number of weeks. Usually they had disappeared after the second month, and always by the end of the third month. Cooke concludes that when an infant's blood gives a positive complement-fixation test for tuberculosis, this reaction is not evidence of tuberculous infection of the infant, since these fixing substances are not formed during the first year of life. The presence of such fixation is noted only when the fixing substances are transferred from the mother. The transmission of complement-fixing antibodies in tuberculosis is not accompanied by a transmission of substances which render the skin sensitive to tuberculin. C. L.

v. Wassermann, A., u. **Ficker, M.** Ueber die Verwendung von frischem unabgebautem Toxin zur Herstellung und Prüfung von Diphtherieantitoxin. [**On the use of fresh unaltered toxin in the preparation and assay of diphtheria antitoxin.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1922, **96**, 1.

Recently a considerable amount has been written against the specificity of diphtheria antitoxin, and it has been alleged by Bingel and others that the results of treating diphtheria cases with normal horse serum are not inferior to those in which diphtheria antitoxin has been employed. It has been alleged that the toxin employed for immunization of horses is not the same poison as that formed in an acute diphtheria intoxication in man. It is this point that the present authors have investigated experimentally. They find that with suitable precautions cultures of *B. diphtheriae* form a potent poison in 24 hours. This poison proved to be identical with the ordinary toxin employed for immunization purposes and was neutralized by antitoxin in exactly the same manner. W. B.

Hansen, T. The influence of the universal light bath on the amount of typhoid agglutinin in human blood, and some observations as to the effect of the light bath on rabbits injected with killed typhoid bacillus. *Acta Med. Scand.*, 1922, **56**, 629.

Hansen's investigations were conducted with a view to ascertaining whether carbon arc light does or does not affect the amount of typhoid agglutinin in the blood. Thirty patients were injected with 1 c.cm. of typhoid vaccine, and some were immediately given exposures to the carbon arc lamp as soon as the rise of temperature, due to the injection, had disappeared. Others were not given light baths till 2 weeks after the injection. Blood samples were taken at first every day and later every other day. For titration, Schroeder's technique was used with a 24-hour broth culture of the typhoid bacillus which was killed by Dreyer's method. After describing the technique adopted with rabbits, Hansen concludes that: (1) the universal light bath affects the normal agglutinin curve, which is replaced either by a plateau or a fall slower than normal, or an

extra rise after the fall has started; (2) rabbits exposed to a light bath tolerate the injection of dead typhoid bacilli much better than control rabbits.
C. L.

BIOCHEMISTRY

VON MEYSENHURY, L. Inorganic phosphate content of breast-milk of mothers with normal and rachitic infants. *Am. J. Dis. Child.*, 1922, **24**, 200.

There is no reduction in the inorganic phosphate content of the breast-milk on which infants develop rickets. Confirms finding of previous observers that the inorganic phosphate of the serum is reduced in rickets.
O. L. V. de W.

EGE, R. Om Bestemmelse af fri og bunden Pepsin i Maveindhold. [**The determination of free and fixed pepsin in the contents of the stomach.**] *Ugesk. f. Læger.*, 1922, **84**, 1227.

Ege's test is a modification of Fuld's edestin test, which, in its original form, is very inaccurate as well as tedious. The principle of the test depends on the fact that a solution of edestin in an acid medium is precipitated on the addition of a neutral salt, whereas the decomposition products following pepsin digestion are not precipitated. The more effective digestion has been, the less will be the precipitate when a known quantity of neutral salt is added. The test may also be carried out by estimating the amount of neutral salt required to give the same degree of precipitation as in the control vessel. Ege has used the latter method. To 10 c.cm. of a 0·2 per cent. solution of edestin there is added from 0·1 to 1 c.cm. of the fluid whose concentration in pepsin is to be determined. The total volume of the solution is now brought up to 11 c.cm. by the addition of from 0·9 to 0 c.cm. of the acid in which the edestin is dissolved. After digestion has proceeded for the desired time (usually half an hour) it is stopped by putting the test-tubes in boiling water for 5 minutes, after which they are cooled, and 1 c.cm. of a 0·5 per cent. solution of gum arabic is added to act as a protective colloid and to prevent the precipitate being too uneven. The salt solution is now run in from a burette until the cloudiness provoked is dense enough to prevent figures or letters being seen through it. As one of Ege's tables shows, from 0·03 to 1 mgm. of pepsin can be determined in this manner, and, by taking 24 hours over the test, it is possible to detect as small a quantity as 0·0001 mgm. of Armour's pepsin.

In diseases of the stomach there appears to be no constant relation between the secretion of acid and of pepsin. In the past, determinations of the acids of the stomach have been given far greater prominence than determinations of the quantity of pepsin present, but the latter may prove of great diagnostic and prognostic value. The quantity of pepsin secreted daily by the stomach is almost certainly not less than the equivalent of 10 gm. of Armour's pepsin. As the quantities of pepsin hitherto given medicinally have been considerably less than 1 gm. a day, this dosage seems timidly futile. It is useless to give pepsin to a patient with achylia unless the acidity of the gastric juice is brought up to the strength required for pepsin to exert its normal action. As the stomach secretes at least 1·5 to 2 litres daily, and as gastric juice contains about $\frac{1}{10}$ n. HCl, it would be necessary in the case of acid-achylia to give 1·5 to 2 litres $\frac{1}{10}$ n. HCl. But in practice the amount of HCl given medicinally in such cases is 83 c.cm. $\frac{1}{10}$ n. HCl, i. e. about one-twentieth of the quantity which the normal stomach secretes. The amount of HCl usually given at each meal is approximately sufficient to neutralize 200 c.cm. of saliva—a quantity secreted at every meal. Even if the usual dosage were doubled, it could not be expected to exert the slightest influence on digestion in true achylia. As a reduction or total disappearance of acid from the gastric juice is far more common than complete disappearance of pepsin, it is of greater importance to institute a rational acid medication than a pepsin medication. Small doses of acid being futile, and the administration of large doses requiring the use of the stomach tube, it would be advantageous if another acid could be substituted for HCl. Ege recommends citric acid, 10 gm. of citric acid being no more difficult to swallow than a $\frac{1}{10}$ n. HCl which has the same hydrogen-ion concentration; yet the capacity of the citric acid to neutralize bases is 300 times greater. A further advantage possessed by citric acid is that it can be given in a pill in such a way that it is not dissolved till it reaches the stomach. The dosage of citric acid would have to be 7 gm. if the acidity of the solution is to be equivalent to the normal HCl acidity of the gastric juice.

C. L.

Molnar, B., u. Hetenyi, G. Über den Chlorgehalt des Blutserums bei Sekretionsstörungen des Magens und Beeinflussung der Anazidität durch Kochsalz. [**Chloride content of serum in secretory disorders of the stomach, and effect of NaCl on anacidity.**] *Arch. f. Verdauungskrankh.*, 1922, **20,** 8.

The authors have noticed an increase in cases of anacidity during the war, which they attribute to a comparatively vegetarian diet and a low intake of NaCl. The serum of cases of anacidity and hyperacidity showed a chloride content falling within the normal limits. The serum of cases of anacidity showed a chloride content tending to the lower normal level: in hyperacidity, the serum chloride was usually at the higher normal level. Anacidity cases showed improvement when treated with NaCl.

V. de W.

Einhorn, M. Weitere Experimente zur Beobachtung der Wirkung verschiedener Salze und anderer Substanzen auf die Leber nach ihrer Einführung in das Duodenum. [**Observations on the action of various salts and other substances on the liver after introduction into the duodenum.**] *Arch. f. Verdauungskrankh.*, 1922, **29,** 243.

The solutions to be tested were introduced through the duodenal tube, and the alkalinity, specific gravity, and colour of the duodenal contents examined at intervals. The increased secretion of bile into the duodenum in response to a stimulus of this type is not due to emptying of the gall-bladder. The reaction is unchanged in character in patients whose gall-bladder has been removed. Also in the case of magnesium sulphate, the stronger the solution, the darker the bile secreted, and an immediate repetition of the test leads to a similar course of colour reaction. Among substances tested, peptone, sodium carbonate, glucose, and pilocarpine evoked a reaction. The most active excitant was a 13 per cent. solution of magnesium sulphate. At operation it was found that the administration of magnesium sulphate in this way did not produce a contraction of the gall-bladder. In jaundice the test may be used to determine whether or not the obstruction is complete.

O. L. V. de W.

Deloch, E. Zur Funktionsprüfung der äusseren Pankreassekretion durch Untersuchung des Duodenalsaftes. [**Investigations on the external pancreatic secretion by examination of the duodenal contents.**] *Arch. f. Verdauungskrankh.*, 1922, **30**, 27.

As a stimulus to secretion 30 c.cm. of decinormal HCl were injected by the duodenal sound, the contents of the duodenum being withdrawn after 5 minutes. Secretion continues for 45 to 60 minutes, and 35 to 65 c.cm. of secretion, mixed with bile, are usually obtained. The physiological stimulus (HCl) produces a larger secretion of juice than does ether, and the juice obtained is richer in ferments. In seven of eighteen cases of hyperacidity, in some of which gastric or duodenal ulceration was present, a hypersecretion of the pancreas was found. In achylia gastrica there is a tendency to compensatory pancreatic hypersecretion. In cholecystitis and diabetes mellitus the tryptic titre of the juice is frequently low. In two cases of pancreatic carcinoma all ferments were much diminished.

O. L. V. de W.

Gerard, R. W. Chemical studies on intestinal intoxication. 1. The presence and significance of histamine in an obstructed bowel. *J. Biol. Chem.*, 1922, **52**, 111.

This represents a further confirmation of the presence of toxins in obstructed parts of the bowel. Histamine is present in isolated closed loops of dogs' intestine. It is apparently produced by bacteria, because it is not found in sterile jejunal secretion. It is, however, found in mucous membrane.

R. A. P.

Meakins, J., and **Harrington, C. R. The relation of histamine to intestinal intoxication. II. The absorption of histamine from the intestine.** *J. Pharmacol. & Exper. Therap.*, 1922, **20**, 45.

The authors have been able to demonstrate the presence of histamine in the contents of the human caecum and tranverse colon. In some of these cases the histamine was still present from the date of the operative relief of intestinal obstruction. If histamine is to be regarded as an active agent in cases of intestinal intoxication it is necessary to postulate that the small quantity formed is quantitatively absorbed, or that after absorption the substance is not susceptible to oxidation in the body as are most compounds of a similar chemical nature. They have undertaken an experiment on the absorption of histamine from different parts of the intestine. The rate of absorption as measured by the fall of blood-pressure is greatest from the ileum, less from the duodenum, and much less from the caecum and the stomach. The liver exercises a protective function, probably more mechanical than chemical, against the toxic action of the base. With the mucous membrane damaged by cutting off the blood-supply for 5 to 15 minutes, the fall of blood-pressure would indicate that absorption takes place at first with a rush and then almost ceases.

C. G. L. W.

Neubauer, E. Beiträge zur Kenntniss der Gallensekretion. II. [**Contributions to the knowledge of bile secretion.**] *Biochem. Ztschr.*, 1922, **130**, 556.

In this continuation of previous work, the original technique with rabbits has been followed. Of various substances tested the following produced a cholagogue effect: bile, the sodium salts of cholic acid and of tauro- and glyco-cholic acids, the ethyl ester and the iodine compound of cholic acid, and its nearest oxidation product dehydrocholic acid. Other substances such as bilianic acid had no effect (constituent of the cholic acid molecule). The strongest stimulant effect was produced by desoxycholic acid, which Pregl has claimed to be a normal constituent of bile. So far as they go they seem to show that the cholagogue effect is correlated with the presence of a monobasic alcohol or keto acid (cholic acid is a monobasic acid containing 3 OH groups). The effect cannot apparently be correlated with the surface activity of the substances in question. R. A. P.

Robinson, C. S. The hydrogen-ion concentration of human faeces. *J. Biol. Chem.*, 1922, **52**, 445.

The normal reaction of human faeces lies between P_H 7·0 and 7·5 (blood reaction 7·35). There is on the whole not much variation. When common laxatives are given the usual result is the production of an acid stool. Strangely enough the bacterial flora of the intestine do not seem to have much influence upon the reaction. The intestine seems able to regulate the production of acid by acidophilic bacteria. R. A. P.

Bornstein, A., u. Holm, K. Über den respiratorischen Stoffwechsel bei alimentarer Glykaemie. [**On the respiratory metabolism in alimentary glycaemia.**] *Biochem. Ztschr.*, 1922, **130**, 209.

When glucose is ingested, a rise in the amount of blood-sugar rapidly appears. The respiratory quotient does not, however, rise for an appreciable time (about 40 minutes after taking the sugar), indicating that burning of glucose does not start concurrently with its introduction into the blood-stream. Laevulose on the other hand undergoes immediate burning upon reaching the blood-stream. This is taken to be evidence in favour of the interesting view that a preliminary conversion of glucose to laevulose is required before utilization by the organism. The ingestion of phosphate simultaneously with the glucose did not lead to a more rapid burning of the glucose, so that no evidence was obtained in favour of a simple phosphate synthesis. R. A. P.

Holst, J. E. Undersögelser over Sukkerindholdet i Cutanblod og Veneblod ved Diabetes mellitus og andre Glykosurier. [**Investigations into the sugar content of cutaneous and venous blood in diabetes mellitus and other forms of glycosuria.**] *Hosp.-Tid.*, 1922, **65**, 577.

In 1921, Hagedorn compared the sugar content of the capillary blood taken from a vein in the arm, and he found that the differences were not the same for diabetics and normal persons. In normal fasting persons the sugar content of the blood, taken simultaneously from these two sources, was practically identical. After the administration of carbohydrates and an increase of the sugar content of the blood, this was less in venous than in capillary blood, the difference in the two concentrations usually being greatest when the concentration of the sugar was highest. In normal persons (64 investigations) the difference ranged from 0·001 to 0·049, with an average difference of 0·026. He could find no regularity in these differences, great variations occurring not only in different persons but in the same person at different times. In diabetics the difference between the sugar content of the capillary and venous blood after the administration of carbohydrates was usually much smaller and was sometimes not demonstrable. The average difference for 26 investigations was 0·010. Hagedorn concluded that the composition of the capillary blood from the ear closely resembles that of arterial blood. Holst has carried his investigations a step further, his material consisting of 14 cases of diabetes mellitus and 23 of other forms of glycosuria. He confirms Hagedorn's finding that in diabetics given carbohydrates there is usually little or no difference between the sugar content of cutaneous blood and that of venous blood. The behaviour in this respect of the 23 patients with non-diabetic glycosuria was essentially that of normal persons. C. L.

Haggard, H. W., and **Henderson, Y. The influence of hydrogen sulphide upon respiration.** *Am. J. Physiol.*, 1922, **61**, 289.

Hydrogen sulphide is frequently found in considerable amount in the intestines, so that perceptible amounts may be excreted in the breath of persons who are virtually healthy. Yet in certain not very high concentrations it acts as an acute poison similar to potassium cyanide. This remarkable paradox is due to the fact that the organism has the capacity to handle H_2S by oxidation up to a certain limit entirely without ill effects. In slightly larger amounts hyperpnoea is induced, followed by apnoea vera, during which the animal dies. This respiratory response is attributed to a stimulation of the afferent endings of the pulmonary vagus. There is no direct effect on the respiratory centre or on the hydrogen-ion concentration of the blood. The latter is affected indirectly, since during the hyperpnoea induced by H_2S a loss of CO_2 occurs. W. C.

Sheaff, H. M. A method for the quantitative estimation of minute amounts of gaseous oxygen and its application to respiratory air. *J. Biol. Chem.*, 1922, **52**, 35.

A new method for the estimation of minute amounts of oxygen is described which claims to be delicate enough to detect amounts of oxygen of less than 0·1 c.mm. of the gas. By the use of this it has been found that 10 mgm. of frog's sciatic nerve uses approximately $0{\cdot}76 \times 10^{-5}$ gm. of oxygen per 10 minutes in the resting state and about double this amount when stimulated by weak induced shocks. The microchemical method depends upon a colorimetric estimation of nitrite formed by the interaction of oxygen and nitric oxide in the presence of sodium hydroxide.

R. A. P.

Greene, C. W., and **Greene, C. H. The partial pressure of oxygen in the blood during progressively induced anoxaemia.** *J. Biol. Chem.*, 1922, **52**, 137.

This paper deals with the debated question of oxygen secretion in the lung. A dog is able to stand the effects of lowered oxygen tension in the inspired air much better than a man. Using dogs, the percentage of oxygen in alveolar air was greatly reduced and the percentage saturation of the arterial blood estimated. No evidence was obtained for the secretion of oxygen. Section of the vagi did not affect the degree of saturation of the arterial blood. R. A. P.

Claudius, M. En Metode til Mikrobestemmelse af Klor i Blod og andre albuminholdige Medier. [**A method for the micro-determination of chlorine in the blood and other media containing albumin.**] *Ugesk. f. Læger.*, 1922, **84**, 1366.

Claudius has devised a method for determining the quantity of chlorine in the blood. It takes only about a quarter of an hour and is not open to the objections raised to the method devised by the late Ivar Bang. A capillary pipette, such as is used for haemoglobin tests, is filled with 20 c.mm. of blood drawn from the ear. The blood is emptied into a test-tube of Jena glass, containing a few drops of water, and the pipette is then rinsed out with a few more drops of water. From a pipette exactly graduated to $\frac{1}{100}$ c.cm. and supplied with a capillary point, 0·2 c.cm. of $\frac{n}{25}$ $AgNO_3$ solution, containing a trace of HNO_3, is added. Then 4 to 5 drops of pure concentrated HNO_3 are added, and the mixture is heated, but not allowed to boil until the coagula have dissolved. The mixture is now boiled over a flame, the test-tube being constantly shaken. This process is continued till the solution has become quite clear except for a trace of silver chloride. The heating is continued until approximately the same volume of fluid has been evaporated as that represented by the addition of the HNO_3. Now one drop of a 4 per cent. solution of $KMnO_4$ is added, banishing the yellow colour. After the mixture has been thoroughly cooled, about 5 c.cm. of pure absolute alcohol and one drop of a 4 per cent. solution of ferric nitrate, faintly acidified by HNO_3, are added. From the micro-burette is now added 0·5 c.cm. of $\frac{n}{200}$ potassium thiocyanate in absolute alcohol. After shaking, the mixture is divided into two small flasks. To the one, the thiocyanate solution is added drop by drop, with constant shaking of the flask, till a faint, permanent rose tinge appears. The colours of the two flasks are compared with a background of white paper. The contents of the first flask are slowly added to the second flask until the colours of the two are identical. The quantity of thiocyanate used is subtracted from the quantity of the $AgNO_3$ solution on $\left(\frac{n}{200}\right)$. The quantity, d, of $\frac{n}{200}$ $AgNO_3$, which is bound to the chlorine, indicates the amount of chlorine present, according to the following formula: $\frac{d \cdot 58{\cdot}5}{2 \cdot 20} = ClNa$ per cent. C. L.

Van Slyke, D. D. Studies of acidosis. 18. Determination of the bicarbonate concentration of the blood and plasma.

Cullen, G. E. 19. The colorimetric determination of the hydrogen-ion concentration of the blood plasma.

Cullen, G. E., and **Hastings, A. B. 20. A comparison of colorimetric and electrometric determinations of the hydrogen-ion concentration in solutions containing carbon dioxide.**

Van Slyke, D. D. 21. On the measurement of buffer values and on the relationship of buffer value to the dissociation constant of the buffer and the concentration and reaction of the buffer solution. *J. Biol. Chem.*, 1922, **52**, 495.

The bicarbonate concentration of the blood circulating in the body can be determined in one of two ways. Either the total CO_2 of the blood or plasma can be estimated, together with the reaction (P_H), (the equation connecting these two is as follows:

$$BHCO_3 = K. \frac{H_2CO_3}{[H+]}),$$

or the plasma may be titrated, using the P_H of the plasma ‘as drawn’ as the end point of the titration. The two methods are described. With certain precautions the titration method would seem to be simple, and the result given compare very well with the gasometric method.

The colorimetric determination of the reaction of the plasma is performed on the diluted plasma, only about 0·5 c.cm. of serum being required. The method does not involve the use of a dialyser. An experimentally determined factor is used to convert the colorimetric reading of diluted plasma or serum at room temperature to the actual reaction of the undiluted plasma, at 38° C., as determined electrically. A comparison of the electrometric and colorimetric determinations for CO_2 solutions left the authors (Cullen and Hastings) with the view that the electrometric method can still be regarded as the standard even where CO_2-containing solutions are used.

Van Slyke's concluding paper of the series is a theoretical one dealing with the conception of the buffer value of a solution. As a numerical measure of this, the buffer value of a solution is defined as the number of gramme equivalents of strong alkali or acid taken up per unit change in P_H (log H-ion concentration). The buffer value of a solution varies at different P_H, as it depends upon the degree of dissociation of the weak acid or base responsible for the buffer action. The value for any given P_H is given by the ratio $\frac{dB}{d\,P_H}$. Starting from this conception a series of equations are developed, expressing various relations for buffer solutions. R. A. P.

Behre, J. A., and **Benedict, S. R. Studies in creatine and creatinine metabolism. IV. On the question of the occurrence of creatinine and creatine in blood.** *J. Biol. Chem.*, 1922, **52**, 11.

This paper raises again the interesting though difficult question of the relation between creatine and creatinine. By the use of the most careful technique the authors have come to the conclusion that there is actually no creatinine present in the blood. The ‘creatinine’ estimated by other methods must be something else. On the other hand, they have obtained definite evidence for the existence of creatine in the blood. It seems, therefore, that the kidney has yet another function, namely, the separation of creatine from the blood as creatinine. In five dogs in which the kidney function was removed by ligature of the ureters, high values of creatine were found varying from 8·9 to 16·8 mgm. per 100 c.cm. This suggests that creatine is a waste product. It is considered that this new evidence must be taken into account in any theory of creatine and creatinine metabolism. R. A. P.

GYORGY, P. Über den Gehalt des Blutserums an Kalk und anorganischem Phosphor im Säuglingsalter. [**Calcium and inorganic phosphate content of the blood in infancy.**] *Jahrb. f. Kinderheilk.*, 1922, **99**, 1.

The conditions influencing the ionization of the blood calcium are discussed. In this connexion the importance of the phosphate and bicarbonate of the blood is emphasized. In rickets the calcium is high in proportion to the phosphate, in tetany the position is reversed.

O. L. V. de W.

EGE, R. Untersuchungen über die Volumenveränderungen der Blutkörperchen in Lösungen von verschiedenem osmotischem Druck. [**Studies of the volume changes of the blood corpuscles in solutions of varying osmotic pressure.**] *Biochem. Ztschr.*, 1922, **130**, 99.

A measurement of the velocity of swelling of red blood corpuscles in solution of ammonium salts has shown that the relative rate of permeability of anions is higher, the smaller the ion. Non-electrolytes, such as urea and ethyl alcohol, do not influence the blood-volume, but there is a marked effect produced by change of reaction. Acidity leads to an increase of blood-corpuscle volume, alkalinity the reverse.

[A similar type of occurrence in the case of human blood has been studied at length by Price-Jones.] R. A. P.

CARRIER, E. B. **Studies on the physiology of capillaries. V. The reaction of the human skin capillaries to drugs and other stimuli.** *Am. J. Physiol.*, 1922, **61**, 528.

In these observations, which were carried out in Krogh's laboratory, the behaviour of the capillaries in the human skin in health was studied by Lombard's method. After placing a drop of paraffin oil on the skin at the base of the finger-nails or on the back of the hand the area was illuminated with an arc lamp and examined with a Greenough binocular. The general conclusion is that the diameter of the capillaries is not necessarily dependent on the pressure in the arterioles but rather on their own tone and contraction. They normally relax or contract independently of the pressure behind them, but in response to local or general stimuli. This constitutes a factor of great importance in the regulation of the circulation. The observations do not support the view that a peristaltic-like activity of the capillaries exists.

W. C.

MEEK, W. J., and **EYSTER, J. A. E.** **The effect of plethora and variations in venous pressure on diastolic size and output of the heart.** *Am. J. Physiol.*, 1922, **61**, 186.

Intravenous injection of acacia saline, physiological saline, or blood in quantities varying from 25 to 103 per cent. of the total blood-volume did not increase permanently the diastolic size of the heart in dogs. The capillaries and venules open up and act as reservoirs and thus prevent a cardiac dilatation or an increase in the volume of the effective circulation.

Immediately after the injection of large volumes of fluid there is an increase in the diastolic size of the heart which runs parallel with the increase in venous pressure until the latter has reached 150 mm. H_2O. Beyond this pressure little effect is produced on diastolic size. This immediate effect, however, passes off in a few minutes. W. C.

Taylor, N. B., and **Cameron, H. G.** **Voluntary acceleration of the heart.** *Am. J. Physiol.*, 1922, **61**, 385.

Cases of direct voluntary control of the heart are rare. The paper records observations on one such case, a healthy young man (one of the authors) who was able to accelerate his heart from about 70 beats to 110 or 120 without any preliminary emotional effort by an effort of the will alone. The interesting manner in which the subject developed this capacity is described. The observations show that acceleration was accompanied by phenomena associated with sympathetic excitation, such as vasoconstriction. elevation of blood-pressure, dilatation of the pupils. Glycosuria also occurred as an after-effect, but curiously enough no change could be detected in the blood-sugar. It is concluded that voluntary acceleration is not due alone to vagal depression as is generally supposed, but also to stimulation of the sympathetic accelerator nerves. W. C.

Abel, J. J., and **Rouiller, C. A.** **Evaluation of the hormone of the infundibulum of the pituitary gland in terms of histamine, with experiments on the action of repeated injections of the hormone on the blood-pressure.** *J. Pharmacol. & Exper. Therap.*, 1922, **20**, 65.

The authors describe a preparation of the pressor-oxytocic principle of the infundibulum which is actually equal to from 20 to 30 times its weight of the acid concentrate of histamine. It is estimated that when the active principle is freed entirely from inert matter it will be found to be, weight for weight, 40 to 50 times more powerful in its action on the guinea-pig uterus than histamine. The hypophysis of the ox does not contain more than 2 mgm. of the oxytocic principle. The solution obtained exhibits all of the really characteristic physiological activities of ordinary saline extract of the infundibulum. The results obtained with relatively pure solution and with the salts obtained from them lead the authors to believe that the vasomotor, oxytocic and renal actions of the preparation are only the expression of the manifold physiological properties of one and the same hormone. In addition to this principle the infundibulum also contains depressor substances which have been described in previous papers. The methods used by the authors in the present work effect complete separation of the pressor-oxytocic substances from these depressor substances.
C. G. L. W.

Carrasco-Formiguera, R. **The production of adrenal discharge by piqûre.** *Am. J. Physiol.*, 1922, **61**, 254.

Puncture of the floor of the fourth ventricle (Bernard's piqûre) sends impulses along the splanchnic nerves and produces amongst other things hyperglycaemia and glycosuria. A large amount of recent work has been done to determine whether the adrenals are involved in these effects. From the fact that hyperglycaemia and glycosuria can be produced by piqûre after excluding the adrenals many observers have concluded that the adrenals are not involved. This conclusion does not logically follow from the observed facts. In the present paper evidence is furnished that piqûre produces a discharge of adrenalin from the adrenals in sufficient amount to produce a general effect on other organs. W. C.

Cannon, W. B., and **Carrasco-Formiguera, R. Studies on the conditions of activity in endocrine glands. IX. Further evidence for reflex and asphyxial secretion of adrenin.** *Am. J. Physiol.*, 1922, **61**, 215.

Further experimental confirmation of Cannon's view that the adrenal can be stimulated to secrete by reflex excitation and by asphyxia.

W. C.

Petersen, W. F., H' Doubler, F. T., Levinson, S. A., and **Laipe, J. E. F. Studies on the Kottman reaction for thyroid activity.** *Arch. Int. Med.*, 1922, **30**, 386.

The reaction depends on the protective power of the serum for silver iodide. With great protective power, the size of the silver iodide particles dispersed in the serum remains small, and the photo-sensitivity of the silver salt is reduced. This is seen in conditions of hyperthyroidism. Fright, thyroxin injections, irradiation, and massage of the hypertrophied gland increase the protective action of the serum, but only after several days have elapsed. The reaction is not therefore direct, but is the result of alterations in cellular metabolism following increased thyroid activity.

O. L. V. de W.

Aub, J. C., Bright, E. M., and **Uridil, J. Studies upon the mechanism of the increased metabolism in hyperthyroidism.** *Am. J. Physiol.*, 1922, **61**, 300.

The increase in metabolism produced by thyrotoxin is not due to muscular activity, muscular fibrillation or increased muscle tonus. It occurs in the absence of the adrenal glands, which are therefore not essential to the maintenance of high metabolic rate induced by thyroxin. It is concluded that thyroxin stimulates resting cells directly to a higher level of metabolism, and the old simile is again brought out that the thyroid secretion acts as a draught to a furnace. The arguments against this view and the fact that the thyroid secretion produces a stimulation of the sympathetic and that the resultant mobilization of the liver glycogen in itself leads to an increased rate of metabolism, are ignored.

W. C.

Grant, S. B. Tetany. A report of cases with acid-base distribution. *Arch. Int. Med.*, 1922, **30**, 355.

Six cases of adult tetany are recorded. Two resulted from therapeutic administration of bicarbonate, three were associated with frequent vomiting and one with hysterical hyperpnoea. In four the carbon dioxide capacity of the plasma was definitely elevated (alkalosis). In one case the serum calcium was found to be on the high side.

O. L. V. de W.

Sanger, B. J., and **Hun, E. G. The glucose mobilization rate in hyperthyroidism.** *Arch. Int. Med.*, 1922, **30**, 397.

The blood-sugar curve, the respiratory quotient and the total metabolism, after ingestion of glucose, were determined in a series of normals, and in ten well-marked cases of exophthalmic goitre. Abnormally high blood-sugar curves, as noted by previous observers, were found in the majority of cases of hyperthyroidism, but strikingly toxic cases may show a normal curve. The rise in the respiratory quotient is more marked after glucose administration in hyperthyroidism than in normal individuals. This increased utilization of carbohydrate along with the high blood-sugar suggests that storage of glucose is deficient in this disease.

O. L. V. de W.

Zandrén, S. Ein Beitrag zur Frage der Bedeutung der pathologischen Aminoacidurie. [**Significance of pathological amino-aciduria.**] *Ztschr. f. klin. Med.*, 1922, **94**, 101.

Total nitrogen, amino-acid N, and ammonia were estimated in urine. In 17 cases without evidence of liver disease the amino N varied from 1·4 to 2·7 per cent. of the total nitrogen (average 2·04 per cent.). In a series of advanced pulmonary tuberculosis, active cases without macroscopic evidence of hepatic lesions showed an average content of 2·26 per cent., cases with fatty liver 4·16 per cent., and cases with amyloid disease 4·9 per cent. Catarrhal icterus and circumscribed liver tumours showed no change in the amino-acid content of the urine, and three cases of advanced cirrhosis showed only a slight rise. In 6 cases of acute yellow atrophy, 5 showed a definite increase in the amino-N percentage. In the remaining case, which ran a comparatively chronic course, the negative findings are ascribed to the presence of regenerative processes in the organ. O. L. V. de W.

Hausmann, T. Die polychemische Urobilinreaktion. Chloroformextraktion nach Behandlung des Harns mit Schwermetallsalzen und Säuren. [**The urobilin reaction. Chloroform extraction after treatment of urine with salts of heavy metals and acids.**] *Ztschr. f. klin. Med.*, 1922, **94**, 12.

On addition of a suitable quantity of 10 per cent copper sulphate solution to the urine, the urobilin can be extracted with chloroform and the urobilinogen is converted into urobilin. The salts of other heavy metals and acids have the same effect. O. L. V. de W.

Addis, T. **Renal function and the amount of functioning tissue.** *Arch. Int. Med.*, 1922, **30**, 378.

The author attempts to deduce the amount of secreting renal tissue by a determination of the ratio $\frac{\text{urea in 1 hour's urine}}{\text{urea in 100 c.cm. of blood}}$ under certain specified conditions. To obtain an approximately constant ratio it is necessary that the kidney should be putting forth something approaching its maximum effort. To produce the necessary conditions, the fasting patient drinks 1000 c.cm. of water, with enough urea to raise the blood urea to a level of 60 to 90 mgm. per 100 c.cm. The rate of urea excretion is then dependent on the concentration of the blood urea, and the amount of secreting tissue. With a constant amount of secreting tissue, the rate of excretion varies directly with the blood-urea concentration. In the rabbit 10 gm. of renal tissue yield a ratio of 1·75 : in adult men with approximately 300 gm. of kidney substance, the ratio should be 52·5. Actually it was found to average 50·4 (163 observations on 31 normals). The standard deviation was ±6·61, and the variability 13·1 per cent. In 33 ratios on a single individual the variability was only 5·1 per cent. For children, in whom the ratio is of course much lower, it is necessary to correct by a curve showing relationships of body-weight to kidney-weight. O. L. V. de W.

Koch, L. M. Chemical investigations of the central nervous system under normal and pathologic conditions. Chemical examination of the central nervous system in two cases of general paralysis. *Arch. Neurol. & Psych.*, 1922, **7**, 488.

Chemical analysis of five parts of the central nervous system in two cases of uncomplicated general paralysis showed the following changes as compared with normal controls. There was a tendency for the water and proteins to increase and for the lipoids to decrease, and a considerable increase in the water-soluble substances, and since the total solids were practically unchanged, these probably compensated for the loss of the lipoids and especially of phosphatids. Of the lipoids, cholesterol showed a relative increase in all parts, except in the cerebrum where it was practically normal. The phosphatids showed a consistent decrease, while the cerebrosids and sulphatids were less changed. This appeared due to the fact that in the brains investigated the white matter was less affected than the grey. The lipoid phosphorus and lipoid nitrogen were decreased, while the extractive phosphorus and extractive nitrogen were increased. These results agree with those previously obtained by other authors. From a comparative point of view, the author points out that general paralysis differs from dementia praecox because in the former the destructive changes affect several constituents, while in the latter, W. Koch found a diminution in the non-protein neutral sulphur fraction in both the grey and white matter of the brain, though the other constituents appeared practically normal. As regards the various parts of the brain in general paralysis, the cortex showed a greater variation from normal than the corpus callosum; the cerebellum and spinal cord showed perhaps less changes than the cortex but more pronounced ones than the corpus callosum, which was the least affected.

C. D. F.

Thalhimer, W., and Updegraff, H. The sugar content of the blood and spinal fluid in epidemic encephalitis. *Arch. Neurol. & Psych.*, 1922, **8**, 15.

Conclusions: (1) The sugar content of the blood and spinal fluid is increased in epidemic encephalitis. (2) The sugar of the spinal fluid appears to increase after a certain amount of blood-sugar has been reached. (3) The hyperglycorrhachia and hyperglycaemia may be due either to the cerebral lesions or to the general infection. (4) There must be a considerable extension of our knowledge of the amount of sugar in the spinal fluid under normal and pathological conditions before the diagnostic significance of hyperglycorrhachia is established. (5) At present hyperglycorrhachia can be used chiefly to differentiate epidemic encephalitis from the two conditions with which it is most likely to be confused, viz. tuberculous meningitis and early poliomyelitis.

C. D. F.

Hartman, F. A. The relation of the adrenals to muscular activity. *Endocrinology*, 1922, **6**, 511.

In normal animals exercise is accompanied by an increased output of adrenalin, which persists for some time after exercise ceases. Intramuscular injections of adrenalin improve the output of work both in normal animals and in animals with adrenal insufficiency.

W. C.

Gruber, C. M. Studies in fatigue. 1. The effect of intravenous injections of massive doses of adrenalin upon skeletal muscle at rest and undergoing fatigue. *Am. J. Physiol.*, 1922, **61**, 475.

Adrenalin injected intravenously increases the height of muscular contraction both in non-fatigued and in fatigued mammalian muscle. With relatively large doses the increase may amount to as much as 240 per cent. in the fatigued muscle, so that the contraction of the fatigued muscle exceeds in height the initial contractions before fatigue. This result is not due to changes in blood-pressure or bettered circulation, nor does adrenalin neutralize or destroy the fatigue products. It acts by increasing the irritability of the muscle. W. C.

Wright, S. Some observations of the nature and significance of the white line of Sergent. [B.] *Endocrinology*, 1922, **6**, 493.

If the skin of a suitable individual be lightly stroked with a round smooth object a white line appears after a definite latent period. It gradually increases in intensity, persists for a minute or longer and then slowly fades. This phenomenon is the so-called 'white line of Sergent', which was taken by him as indicating adrenal insufficiency and this interpretation has received support from other observers. The present paper contains observations on 100 normal individuals. It is shown that 'the white line' is a phenomenon occurring in a large number of healthy subjects and has no pathological significance. It is produced by local emptying of the capillaries and is probably a nervous mechanism of the nature of an axon reflex. W. C.

Lee, O. P., and **Tashiro, S. Studies on alkali genesis in tissues. II. Ammonia production in muscle during contraction.** *Am. J. Physiol.*, 1922, **61**, 244.

Tashiro has shown previously that frog's nerve gives off ammonia in small amounts. In this paper it is shown that frog's muscle also gives off ammonia in exceedingly small amounts and that this amount is about doubled during contraction. The amount given off by muscle is much less than that given off by nerve—the proportion being 1 : 14 for the same unit of weight. The amount is too small to produce a distinct effect on the total nitrogen excretion. W. C.

Talbert, G. A. Further studies in the hydrogen-ion concentration of human sweat. *Am. J. Physiol.*, 1922, **61**, 493.

Very few observations have been made on the reaction of human sweat and the few recorded observations are contradictory. Human sweat has an acid reaction; the average hydrogen-ion concentration is $P_H = 5 \cdot 65$. The reaction is due partly to the presence of volatile acids. The reaction of sweat is the same whether sweating is induced by heat or by exercise, but it differs slightly in different regions of the body. Thus the leg gives sweat with a slightly higher acidity than the arm or the face. W. C.

Gramén, K. Untersuchungen über den Äthergehalt in Blut, Milch, Harn und Expirationsluft bei chirurgischer Äthernarkose sowie über Narkoseazidose. [**Investigations into the ether content of the blood, milk, urine, and expired air of the subjects of ether anaesthesia. Also concerning the acidosis of general anaesthesia.**] *Acta Chir. Scand.*, 1922, **55**, pp. **146**. (Published as a supplement.)

Gramén has carried out about 700 quantitative ether analyses on human beings, using a modification of the bichromate test for the quantitative estimation of the ether in the fluids of the body. Under ordinary conditions the ether content of the venous blood rises to about 80 mgm. per cent. within about 10 to 12 minutes of the first administration of ether. It remains at this level throughout the rest of the anaesthesia with only slight variations. After ether has been given for about 30 to 60 minutes, and is then discontinued, the ether content of the blood falls during the next 15 minutes to about half its previous level. But the total elimination requires 1 to 2 days, and the rate and duration of elimination are directly proportional to the quantity of ether given. No exact figure could be obtained to show the quantity of ether excreted by the kidneys. The amount eliminated in the expired air during the first 10 minutes after the discontinuation of the anaesthetic is 28 mgm. ($2\frac{1}{5}$ drops) of ether per litre of air. When ether is demonstrable in the milk, it is in almost as high a concentration as in the blood. Analysis of the air expired by the anaesthetist, after he had administered ether for a single operation of moderate length, showed that in about 2 minutes he had eliminated 1 drop of ether. In this connexion Gramén discusses the dangers of chronic ether poisoning for anaesthetists, and he compares this danger with that of chronic alcoholism.

Quantitative analyses of the total acetone and of the β-oxybutyric acid in the blood and urine of 12 non-diabetic patients, to whom ether had been administered, showed that, with only one exception, there was an increase of the β-oxybutyric acid in the blood. In most cases this increase was slight, but in 1 case, associated with 'operation shock' it was as high as 75 mgm. per cent. during, and as high as 93 mgm. per cent. immediately after, the administration of ether. Among non-diabetic cases, ketonuria was found before the operation in 9·9 per cent., and after the ether anaesthesia in 67·7 per cent. After novocaine anaesthesia it was found in 9·1 per cent. Turning to the practical lessons to be extracted from his investigations, Gramén considers injurious the administration of purgatives and the withholding of food in connexion with ether anaesthesia. To combat the acidosis it provokes, glucose and bicarbonates should be given, and the supply of fluids should be ample. As ether anaesthesia is apt to induce achylia, it is advisable to give citric acid or hydrochloric acid.

C. L.

Walbum, L. E. Studien über die Bildung der bakteriellen Toxine. II. Diphtherietoxin. [**Studies on the formation of bacterial toxins. II. Diphtheria toxin.**] *Biochem. Ztschr.*, 1922, **130**, 25.

For the production of the maximum possible amount of toxin, it is important to attend very carefully to the conditions of culture. The diphtheria bacillus grows between the limits P_H 5·2 and 8·90, the optimum being at P_H 7·0. Diphtheria toxin is destroyed in acid or alkaline solutions, the optimum for stability being at P_H 7·2. The optimum temperature for the formation of the toxin is 36° C. The actual toxin present in a culture is the balance between the amount formed and the amount destroyed. The preparation of the culture medium (veal bouillon with peptone) must be accurately done. Chloride content, for instance, makes a difference, and a trace of $MnCl_2$ improves the yield. R. A. P.

Stepp, W. Über die Bedeutung des Dimethylhydroresorcins für die Unterscheidung flüchtiger Aldehyde in Körperflüssigkeiten. **[On the importance of dimethylhydroresorcin for the differentiation of fluid aldehydes in the body fluids.]** *Biochem. Ztschr.*, 1922, **130**, 578.

In a case of contracted kidney, the amount of acetaldehyde upon certain days showed enormous increases above a normal value. This led to an attempt to identify the acetaldehyde by the aldehyde reagent dimethylhydroresorcin. To the surprise of the author the condensation product found was not an acetaldehyde compound. Eventually it proved to be a formaldehyde compound, the formaldehyde having arisen as the result of doses of urotropin. R. A. P.

Günzburg, L. Über Theobrominausscheidung und Theobromindiuresis. **[On theobromine excretion and theobromine diuresis.]** *Biochem. Ztschr.*, 1922, **129**, 549.

By the use of a new method of estimating small quantities of theobromine, a purine derivative found in tea, it is shown that the excretion of ingested theobromine shows a characteristic curve. The maximum takes place in the third or fourth hour after taking the substance, and then falls quickly. By giving alkali at the same time, theobromine diuresis is reduced, whereas it is increased by a simultaneous dose of acid. Chronic caffeine ingestion lowers the sensitivity for theobromine, so that higher doses have to be given to produce diuretic effects. R. A. P.

Storm van Leeuwen and **Szent Györgyi, A. V. On the influence of colloids on the action of non-colloidal drugs. V. A further analysis of the augmentor effect of lecithin on the action of pilocarpine.** *J. Pharmacol. & Exper. Therap.*, 1922, **20**, 1.

The work done during the last few years has shown that the extent of the action which a certain quantity of the drug exerts after injection into an animal may be largely influenced by the presence in the blood of substances which are able to inhibit or augment the action of the drug.

The authors give a short account of the various augmenting actions which are to be found in the literature.

In a previous paper they tell of the augmentor effect of lipoids on the action of pilocarpine and histamine on the isolated gut. In using lecithin they found that the action was very inconstant and in some cases the lipoid refused to act. In the present paper they show that the samples of lecithin with which they dealt contained a large amount of kephalin which is known to have a strong augmentor effect on pilocarpine. The action of pilocarpine can always be augmented by the addition of a small amount of kephalin. Pure lecithin has no influence on pilocarpine action. Histamine is mostly augmented by the addition of pure lecithin, and the influence of kephalin on pilocarpine action is also positive. The action of pilocarpine was not augmented by lecithin but was sometimes increased by kephalin and its ultra filtrate. They believe that kephalin emulsions contain at least one substance which augments the choline and pilocarpine action on smooth muscle, and one substance which stimulates the gut. It is probable that these two substances are not identical. C. G. L. W.

Hardikar, S. W. On rhododendron poisoning. *J. Pharmacol. & Exper. Therap.*, 1922, **20**, 17.

The active principle of the rhododendron, the leaves of which have caused cases of poisoning among sheep, is andromedotoxin. This is a non-nitrogenous compound which may cause death in two forms. With the first, death occurs rapidly and is due to a direct action upon the heart, the ventricles being arrested in diastole or partial systole. With smaller doses it is due to failure of the respiration through a paralysis of the phrenics and often of the diaphragmatic muscle also. There is a narcotic action upon the higher centres in the brain, while the spinal cord is not affected. A part of the poison when injected hypodermically leaves the body unchanged in the urine. C. G. L. W.

Burton-Opitz, R. A comparative study of the different methods of artificial respiration. *Am. J. Physiol.*, 1922, **61**, 562.

Observations on young men, and on cats and dogs to test the efficiency of the various methods of artificial respiration. Schäfer's prone pressure method was found to be the most efficient one. To increase the efficacy of the method it is recommended to place a wedge-shaped cushion, about 8 cm. in thickness, transversely across the abdomen so that the umbilical region of the patient rests on its rounded ridge. W. C.

RADIOLOGY AND ELECTROLOGY

Radiotechnique

Sicart et **Forestier**. Méthode générale d'exploration radiologique par l'huile iodée (lipiodol). [**General method of radiological exploration by means of lipiodol.**] *J. de radiol. et d'électrol.*, 1922, **6**, 390.

Lipiodol, which is a mixture of iodine and poppy oil, contains approximately 0·54 gm. of iodine per c.cm. It is a substance which is both liquid and weighty, and lends itself admirably to the exploration, in absolute safety, of organic cavities. It is extremely opaque under the X-rays, is neither caustic nor toxic, absolutely stable, and capable of prolonged visibility. It is by virtue of its diagnostic and therapeutic value that the authors have investigated the action of lipiodol.

In the first instance they injected it into the epidural cavity in cases of lumbago, lumbar arthritis, and sciatica, and they were able to obtain extremely interesting radiographic images. They also injected it into the cerebrospinal fluid, and even under the cerebral arachnoid; into fistulous channels, hydrarthroses and urethral strictures. But the main study of this process was undertaken in connexion with the tracheo-bronchial tree. In normal conditions, iodized oil, when injected into the air passages, distributes itself according to the laws of weight, and fills those bronchial tubes which terminate in the lower lobes of the lungs: and the delicate tracery is reproduced on the negative.

One understands readily how in a large number of lung cases, the injection of lipiodol may lead to the detection of various noteworthy complications.

Whereas in the majority of organs lipiodol is not only not absorbed, but gives radiographic images lasting for months without deterioration, the same cannot be claimed for the lungs. In them the image fades owing to the elimination (by the urine) of the iodine. However, this urinary elimination remains insignificant as long as radiography reveals in the lungs the presence of small foci of the substance. M. B. D.

Mutscheller, A. Nouveau tube à rayons X. [**A new X-ray tube.**] *Arch. d'électric. méd.*, 1920, **28**, 325.

The new X-ray gas tube is one in which nitrogen is the residual gas. The special feature of the bulb is the gas regulator. The regulating substance consists of a mixture of thorium, barium, and aluminium nitrites which, under the action of an electric spark, emit pure nitrogen. The gas regulator therefore consists of a reservoir of this mixture and an electrode which offers alternative paths to the current through the tube. The current passes through the reservoir, liberating nitrogen in proportion to its intensity, when the bulb is hard, but chooses the alternative path when the latter is soft. There is no dissipation of the regulating substances, for, in periods of rest, the nitrites absorb nitrogen and, at the same time, the bulb retrieves its initial hardness.

The cathode of the tube is surrounded by a steel cylinder serving to focus the cathode rays upon the anticathode and to collect those emitted from the sides of the latter. L. H. C.

Riquard, M. R. Indications anormales fournies par les radiochromomètres avec les rayons X. [**Abnormal indications of penetrometers exposed to very penetrating X-radiation.**] *Arch. d'électric. méd.*, 1920, **28**, 330.

The author found that, whereas the Benoist hardness numbers for the ordinary gas tubes vary from 3 to 7·5, the number for the radiation emitted by a Coolidge tube, fed at a considerably higher voltage, was never greater than 7. Further elevation of the tube voltage lowered the hardness number.

The principle of the Benoist penetrometer has been tested over a wide range of tube voltages and the hardness number is found to reach a maximum, corresponding to a tube voltage of 60,000, and to decrease as the latter potential is exceeded.

The transmission of X-radiation through increasing numbers of silver and of aluminium sheets has been measured, when the source of radiation was a Coolidge tube operating at 88,000 volts. For both metals the penetration increased with increasing thickness. Comparison of the Benoist numbers for the radiation, unfiltered and filtered through three sheets of silver, each 0·11 m.m. thick, shows, in the case of the latter, a decrease of 10 per cent. It is suggested, therefore, that the use of penetrometers of the Benoist type should be restricted to the measurement of medium or soft radiation. L. H. C.

Nogier, T. La 'paraffine armée', substance plastique pour la curiethérapie de surface. [**'Re-inforced paraffin', a plastic substance for surface radium therapy.**] *J. de radiol. et d'électrol.*, 1922, **6**, 423.

The supporting substance chosen by the author is wool felt which is used in the making of spongy electrodes for electrotherapy: this is mixed with paraffin wax, m.pt. 62° C., 100 gm., pure white beeswax 80 gm. The paraffin wax and beeswax are melted in a large aluminium dish, the layer of felt is placed in and all air pressed out of it; it is then lifted out, quickly drained, and placed firmly on a moistened flat slab. This causes the lower surface to solidify and by running water on the upper surface this solidifies also: as the wax in the middle is still soft if not liquid, the whole can be moulded over any desired surface. When cold the mould is quite firm. The following are the advantages claimed for the reinforced paraffin: (1) having no metal there are no secondary β-rays; (2) it acts as a diffuser; (3) it is very light; (4) straps, &c., can be very easily fixed; (5) it is a solid foundation on which the radium carriers can be fixed; (6) it can be worked in the cold with a knife and is easily pierced; (7) it can be used over and over again; (8) the preparation is carried out with the minimum loss of time. P. L.-B.

Ducci et **Kaplan.** Nouvelle méthode d'investigation des contrastes radiographiques. [**A new method for investigating radiographic contrasts.**] *J. de radiol. et d'electrol.*, 1921, **5**, 127.

The authors describe a method for obtaining magnified radiographs of an organ, suitable in cases where its detailed contour, rather than its dimensions, is required. Their apparatus is based upon the property of divergence possessed by X-rays emanating from a point. It consists of a framework supporting three parallel, lead-lined partitions, each containing a rectangular aperture. The distance between the partitions, the sizes, and the relative positions of the apertures they contain, are such as to allow a pyramidal cone of X-rays to pass from the anticathode to the plate support, 150 cm. distant.

The use of three such diaphragms between the plate and the X-ray tube materially reduces the quantity of scattered radiation reaching the former, thus producing a 'clear' image. Further, the apparatus permits of two different magnifications of the object radiographed. L. H. C.

Radiodiagnosis

Wilsey, R. B. The efficiency of the Bucky diaphragm principle. *J. Röntg. Soc.*, 1922, **18**, 77.

The efficiency of the Bucky diaphragm in removing scattered radiation has been measured for a variety of widths and depths of slit. The procedure adopted was to measure the relative intensities of diffuse and focal radiation transmitted by a 6-inch depth of water to a single slit, the dimensions of which could be altered. With a target-slit distance of 25 inches, a tube voltage of 60 kilovolts, and a tube current of 4 milliamperes, the following data were obtained:

1. The ratio of the diffuse to the total radiation is approximately independent of the distance, when small, between the slit and the scattering material.

2. The intensity of the scattered radiation is determined by the ratio of width to depth of slit and not by the actual dimensions of the latter.

3. The efficiency of commercial models of the Bucky diaphragm, defined by the fraction of the diffuse radiation removed by them, ranges from 80–86 per cent.

4. The wood filter used to support the lead strips of the diaphragm is without effect upon the efficiency of the grid, when the slits are small.

To determine the definition obtainable with the diaphragm, a card carrying a set of wire gauzes of differing mesh was used as the test object. For maximum definition, it was found, the slit should be as shallow as possible and at the same time maintain an efficient ratio of slit width to slit depth. Further, for a given slit the definition decreased with increase in the distance between the test object and the slit. L. H. C.

TSCHEBULL, H. Eine neue Darstellung der Nebenhöhlen. [**A new method of demonstrating the accessory nasal sinuses.**] *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1921, **28**, 222.

The method described is a modification of Lilianfeld's technique. The patient lies prone with the arms flexed and the hands crossed under the chest. Artificial teeth are removed and the mouth kept open as widely as possible by a wooden prop. The chin and nose rest upon the plate, with the upper incisors at its centre. The plate is tilted at an angle of 30° with the horizontal, and rests upon a wedge-shaped support. The central ray, from the tube placed above the couch, enters at the vertex and falls perpendicularly to the plane of the top of the couch, striking the plate at an angle of 60°. The head is steadied by means of a bandage over the vertex, and a compression cylinder is used. The tube is somewhat harder than is used for the ordinary antero-posterior view, the time of exposure is doubled or an intensifying screen used.

The radiograph thus obtained gives a clear view of the bones of the face, full of detail and without overlapping shadows. It is, however, not well adapted for demonstrating the details of the ethmoid.

A short bibliography of German work is appended. E. M. W.

STROM. Über die Röntgendiagnostik intrakranieller Verkalkungen. [**On the radiodiagnosis of intracranial calcareous deposits.**] *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1919–20, **27**, 577. (*J. d. radiol. et d'électrol.*, 1922, **6**, 87.)

Intracerebral new growths are only visible in radiographs when they contain calcareous deposits: they can also give evidence of their presence by causing deformities in neighbouring bones. Normally small calcareous deposits can be found in the choroid plexus, the falx, Pacchionian granulations and pineal body. Under pathological conditions calcified tumours may be of different natures: (1) *Benign tumours*, encapsuled or non-encapsulated, with no tendency to enlargement, arising from the periosteum of the base of the skull and situated in any part of the brain. The author makes personal observations on a benign tumour with calcareous deposits arising after a contusion and giving rise to symptoms of Jacksonian epilepsy. (2) In the case of *malignant tumours* endotheliomata and sarcomata are met with, and the author puts forward two personal observations. *Tumours of the hypophysis* form a separate and interesting group; they are usually epitheliomata of the glandular portion and often contain calcareous deposits of various sizes. These tumours are sometimes outside, but more often inside the sella turcica, and in the latter case deform the bony cavity. Gliomata and cysts rarely contain calcareous deposits. (3) *Tuberculous lesions* in the brain, and especially large isolated tubercles, may contain large, irregular, calcareous deposits. (4) *Aneurysms* sometimes contain calcareous deposits. S. E. L.-B.

Heissen, F. Zur Kenntnis der allgemeinen Periostitis hyperplastica des Kindesalters. [**On the diagnosis of general hyperplastic periostitis in childhood.**] *Fortschr. a. d. Geb. d. Röntgenstrahlen.*, 1921, **28**, 239.

Hyperplastic periostitis was first described by Marie under the name of Ostéoarthropathie hypertrophiante pneumonique, as a secondary hyperostosis of the bones of the extremities accompanied by organic changes in the joints and resulting from chronic pulmonary infection. Further investigation showed that the condition followed upon a number of other diseases, of which the most important are chronic purulent processes, chronic intoxications, especially syphilis, and malignant tumours. Cases have also been described where a widespread hyperostosis developed without any demonstrable cause. Curschmann has described a congenital case of this type. According to the literature—not very extensive—the condition very seldom occurs in childhood. The author gives full details of a case where extensive hyperplastic osteitis followed resection of rib for empyema following pneumonia at the age of 4 years. The parents took the child home before the operation wound was healed, and first sought advice eight years later for a small fistula which had persisted the whole time. Nothing in the history was suggestive of rickets, tuberculosis, or congenital syphilis. Clubbing of fingers and toes had been noticed a year after the operation. The child was physically undeveloped, but mentally about the average for his age. The trunk was stunted and deformed, and contrasted with the noticeably long limbs, the distal parts of which were somewhat suggestive of acromegaly in appearance. The hands and feet were markedly affected, and the distal ends of the long bones involved to a less extent. X-ray examination showed uniform enlargement of the phalanges of the hands and feet in both length and breadth. The bone structure appeared normal, and there was no evidence of thickening from a calcifying periostitis. Hypertrophy of the bones of tarsus and carpus was similar in character, but less in degree. The distal ends of the bones of the forearms were similarly involved, the enlargement here being more marked in breadth than length, and the shaft and proximal ends of the bones little affected. The malleoli were markedly club-shaped. The femur and humerus showed less hypertrophy, the condyles being enlarged in width only, and the proximal parts of the bones remaining uninvolved. The movements of the joints were all quite free. The bones of the skull, thorax, and pelvis were normal—and no abnormality was detected in any epiphysial cartilage. As compared with a normal child of the same age, increases in various measurements were noted as follows: length of thumb and middle finger 0·5 cm. to 0·75 cm., forearm and leg 1·0 cm., arm and thigh normal length, length from trochanter to sole 1·0 cm., circumference of ankle at the malleoli 3·0 cm., circumference of wrist round the radial and ulnar epiphyses 2·0 cm., circumference of condyles of humerus 1·0 cm., and of femur 0·5 cm. On the other hand, the circumference of the limbs at the middle of the long bones was 3·0–5·0 cm., less than normal owing to the poor muscular development.

The description here given differs in important particulars from that of the adult cases found in the literature. In the latter a calcifying periostitis occurs, and the long bones chiefly are affected, the changes involving the middle of the shaft rather than the ends of the bones. Massalonga and Gasperini, however, describe the case of a tuberculous boy of 18 years, who had from the age of 5 years a stationary apical lesion of the lung, and in whom clubbed fingers had developed at the same age. Radiographs showed a true hypertrophy of radius and ulna, tibia and fibula, and metacarpus and metatarsus. The same type of bone lesion appeared in Curschmann's congenital case.

It would appear, therefore, that the lesions occurring in adults differ markedly from those found in children, and the latter would be best described as secondary hyperostosis or secondary osseous hypertrophy.

E. M. W.

Radiotherapy

Edling, L. Résultats de notre traitement de la lymphadénite tuberculeuse par les rayons X à Lund de 1908 à 1918. [**The results of treating tuberculous lymphadenitis by X-rays at Lund from 1908 to 1918.**] *Acta radiolog.*, 1922, **1**, 455.

The author states that although lymphadenitis is part of a general disease, from the clinical point of view it is in many cases local or limited in extent and is often the only external manifestation of the disease, and local treatment plays the principal part, particularly in cases where the glands of the neck are involved. The paper deals solely with the local and specific treatment, and the author limits himself to cases of tuberculous lymphadenitis of the neck from 1908–18. In the early days the treatment was entirely surgical, usually the complete removal of the glands, sometimes conservative methods combined with the injection of substances such as iodoform, &c. In 1908, at Lund, 7 per cent. of the operations were for tuberculous adenitis; in 1918 the number had fallen to 1 per cent.; this was due to the advent of radiotherapy. From 1909–12 the author used a modification of Kienboeck's method, which he describes; in 1913 penetrating therapy was introduced by the Fribourg school, and for two years the author used a transition method, and in 1914–15 definitely adopted the deep therapy. Filtration was increased to 3 or 4 mm. of aluminium and also a secondary filter used. Sabouraud's reaction, controlled by Holzknecht's scale, was used to measure dosage, and later the intensimeter of Fürstenau. Generally, children received two to three Holzknecht's units, with three to four weeks between treatments; reference is made to the dosage advised by other workers.

In grouping his cases the author follows the terminology used by Mest: the first phase of a simple hyperplasia of the tuberculous glands followed by the second phase of masses of glands with periadenitis but no suppuration, and lastly a third phase with suppuration, fistulae, &c. A short account of the action of the rays on the glands and the effect on the body generally is given. As regards cases in the first phase usually there is a slight initial reaction, swelling of the irradiated part, occasionally redness and sometimes slight fever. The therapeutic action is seen in the diminution of the glands, which the author states is slow in appearing: it is produced most quickly in soft rapidly-growing glands, and is independent of their size. Long-standing cases are often a long time before they disappear, no doubt on account of advanced induration: in these cases the author leaves intervals up to six months between irradiations to avoid fatiguing the skin. In the majority of cases the end result is a hard fibrous nodule, varying in size from a grain of wheat to a nut, which cannot be further affected. The duration of treatment for these cases is estimated by the author to be 6½ months. As regards cases in the second phase, the author believes them to be more difficult to treat than the above: the periadenitis often disappears quickly, the individual glands can then be felt, they diminish in size and even disappear. In cases of this sort in all probability the histological picture shows chiefly hyperplastic lymphoid tissue and tubercles. In other cases after many years' treatment the action of the rays has only been partial; in these one would suspect fibrous induration or caseous necrosis. The duration of treatment varies greatly; the author gives it at approximately eight months. The third phase, according to the author, comprises the largest number of cases. If a gland has a tendency to suppurate, radiotherapy hastens the commencement of suppuration. In many cases in which suppuration has occurred, perhaps after a single séance, the author can only regard the radiation as the cause. In favourable cases if suppuration occurs he incises the skin, and after further irradiation the secretion becomes more and more serous and finally suppuration ceases. In many cases, however, suppuration continues, and in these an incision is made and the caseous material thoroughly scraped out: X-rays then seem to result in the gland capsules becoming detached and able to be removed. If fistulae exist from the onset the author begins treatment by curetting away the masses of glands; the wounds clean up under radiation and heal quickly in most cases. The cicatrices are claimed to be better than those following surgical measures. On the average, 8–10 months' treatment is necessary for this phase. The author next speaks of what he describes as 'delayed suppuration'. In eight cases he has seen an abscess occur from eight months to five years after the end of the treatment, with no visible cause to account for it.

The author then tabulates his results of the last ten years, and compares them with the statistics in the literature of the same period, and also with Iselin's results for 1908–14: he also refers to the results obtained by surgery. Reference is also made to the risks attached to X-ray treatment and to Iselin's work on the same.

The last group of cases mentioned is one in which 36 patients suffered from atrophy of the skin and 8 from pigmentation: the causes of these accidents are discussed, and mention is made of the fact that for 3½ years there has been no case of skin atrophy following treatment.

In conclusion the author discusses the advantages and disadvantages of X-rays as compared with surgery, and thinks that the advantanges outweigh the disadvantages. He believes that every patient should have the two sides of both methods explained. P. L.-B.

Radiobiology.

Werner, P. Zur Kenntnis der Generationsvorgänge nach der Röntgen- und Radium-Tiefenbestrahlung. [**Influence of deep radium and X-ray treatment on the process of reproduction.**] *München. med. Wchnschr.*, 1921, **68**, 767. (*Am. J. Obst. & Gynec.*, 1922, **4**, 332.)

Stenger. Pregnancy and birth after X-ray treatment of the myomatous uterus. *Schweiz. med. Wchnschr.*, 1921, ii, 1084. (*Am. J. Obst. & Gynec.*, 1922, **4**, 334.)

Aschenheim, E. Danger of X-rays to foetus. *Arch. f. Kinderh.*, 1920, **68**, 28. (*Am. J. Obst. & Gynec.*, 1922, **4**, 334.)

I. It seems to be agreed that deep radiation does not inhibit the power of conception, disturb parturition, or predispose to abortion or premature labour. The fate of the children of women thus irradiated is not so certain: some authors state that varying degrees of montrosities result, others disagree with this view entirely. The author gives the results in a series of 1,512 cases treated by X-rays or radium: 24 pregnancies subsequently occurred; of these, 13 were full time with a living child, 1 four weeks' premature labour, 9 abortions from the second to fifth month, and 1 terminated by hysterectomy for myomata. Of the abortions 3 were induced, 6 spontaneous. All labours were normal; eclampsia developed in one case during labour. All the children appeared normal at birth: 4 have died, the premature in 8 hours from general weakness, and the other 3 from intercurrent disease. Of the living children, 6, between 2 months and 3 years, seem normal mentally and physically; 4, between 6 and 8 years became deficient in height and weight in the fourth and fifth year. In two other cases treatment was continued after the onset of pregnancy: the first went to term and was delivered of a fully-developed and apparently normal child; the second went 4 weeks over time and was delivered of an undeveloped child about 18 inches in length, weighing about 4½ lb. The author's conclusions are that after X-rays or radium pregnancy can occur, that there is no special danger to pregnancy or labour, that a tendency to abortion exists and that the child appears normal at birth, but that later on development appears to be retarded.

II. Stenger describes cases in which apparently healthy children were born after the uterus had been irradiated for large myomata which disappeared; he concludes that impregnation had occurred before treatment or close to it, or else that some of the primordial follicles were immune to the dose used or not reached by the rays. He suggests that amenorrhoea may come on a month or two before sterilization has taken place. If the patient be pregnant before treatment there is no reason to expect either abortion or a maldeveloped child. Apparently the best time to attempt temporary sterilization is the first half of the intermenstrual period.

III. Aschenheim describes a child 3½ years old, that was microcephalic with marked ophthalmic abnormalities. The mother was not syphilitic. He believes two X-ray treatments in the first month of pregnancy to be responsible for the defects in the child.

With reference to this question readers should refer to the paper by Halsey Bagg, abstracted in *Medical Science*, 1922, **7**, 174. P. L.-B.

Electrotherapy.

Laquerrière et Delherm. L'électroradiologie dans le traitement des algies. [**The electro-radiological treatment of neuralgic pains.**] *J. d. radiol. et d'electrol.*, 1922, **6**, 249.

In this excellent general survey the authors point out that the variety in the methods of applying electricity (directly or indirectly) to the many sufferers from neuralgic pains who present themselves for treatment is necessitated by the very diversity of the cases themselves.

1. *Methods of treatment re-acting on the general bodily health.* (*a*) High frequency applications. (*b*) Static bath.

2. *Counter-irritative treatment.* Counter-indicated during the acute period of neuralgia. Static spark. (*a*) Local high frequency applications. (*b*) Hot air percussion. (*c*) Faradaic revulsions.

3. *Re-educative methods of treatment.* Faradaic revulsions by means of Duchenne's brush and Tripier's rake.

4. *Sedative methods of treatment.* (*a*) Douche of warm air (no pressure). (*b*) Electric spray. (*c*) Radiotherapy. (*d*) Continuous current.

5. *Methods of treatment having regard to the cause of the pain.* Neuralgia of nerve trunks gives way especially easily to continuous current, and neuralgia arising in nerve roots to radiotherapeutic treatment; there are known cases in which a combination of both has yielded excellent results.

Lastly, 'tic douloureux' or facial neuralgia can be both relieved and cured by the application of continuous current. It must be understood that the strength and length of the treatment must be adequate, and that the treatments must be persevered with. M. B. D.

Vinay, A. Modifications hématiques et circulatoires produites par la diathermie. [**Modifications (haematic and circulatory) arising from treatment by diathermy.**] *J. d. radiol. et d'électrol.*, 1922, **6**, 248.

The author gave diathermic applications successively to the region of the spleen and to the long bones.

The results were as follows:—Hyperaemia appeared first in the region of the application and gradually all over the body. The temperature (axillary) rose from 1° to 1·5° according to the length and strength of the application. The application, to the splenic region, of, say, 0·7 to 2·5 A. lasting from 15 to 30 minutes, provokes a diminution of arterial pressure and a slight increase in haemoglobin and in red corpuscles. The number of neutrophile polynuclears diminishes, whereas there is an increase in that of the large mononuclears and the transition forms. Contemporaneously to this there is the appearance of myelocytes. A current of 0·5 to 1·15 A. applied to the bones tends to accelerate both radial pulse and respiration. The haemoglobin index rises. There are, therefore, to be observed a group of modifications all tending to prove the existence of a functional stimulus of the leucopoietic tissues when submitted to diathermic treatment.

M. B. D.

Duhem. Action de la diathermie sur l'hypertension artérielle. [**Diathermy: its action on arterial hypertension.**] *J. d. radiol. et d'électrol.*, 1922, **6**, 248.

The author applied to the breast and back of his patients two large electrodes (each about 40 cm. square) leaving them in position for from 20 to 25 minutes. (Intensity 1800 M.A.). In the case of the first patient (age 60) the blood-pressure changed from 21 to 14 after a few treatments given at irregular intervals, and subsequently remained at 15½ to 16. Since then the author has treated 14 other patients in the same way. He was successful in all these cases but one, and that particular patient was albuminuric. In the 13 favourable cases no more than three or four treatments were needed to produce satisfactory results, which still persisted at the end of three months.

Duhem's opinion is that diathermy acts by promoting vascular dilatation. M. B. D.

MEDICAL SCIENCE

ABSTRACTS & REVIEWS

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NOTICE.

In the references the letter [B] after the title signifies that the original memoir contains a good bibliography of the subject dealt with.

REVIEWS

DIABETES MELLITUS

Epidemiology. Hoffman, consulting statistician to the Prudential Insurance Company of America, has drawn up a table of diabetes death-rates for specified countries, in most cases for the five years ending 1919, showing that the range in frequency varies from a maximum of 38·4 per 100,000 of population in the case of the Island of Malta, 18·1 for the Isle of Man, and 16·1 for the Island of Guernsey, to a minimum of 1·5 for the Island of Jamaica, 1·1 for the Bahamas, and 1·0 for Venezuela. The average diabetes death-rate for the United States registration area is 16·4 per 100,000 of population, practically the maximum rate attained by the countries or islands which rank highest in the table. The American death-rate is decidedly above the average of 11·8 for England and Wales, and while it is unquestionably affected by the relatively large Jewish population in the large cities of the United States, this factor cannot be considered as primarily responsible for the marked excess. As regards the mortality from diabetes in cities, the normal diabetic death-rate of New York city for the five years ending 1919 was 19·8 per 100,000 of population, or higher than the maximum rate reported for the city of Berlin (17·9), Copenhagen (17·1), or Amsterdam (15·9). The minimum rates were reported for Tokio (4·1), Singapore (4·3), Manila (4·5), and for the city of Mexico (5·4).

Joslin (1) states that since 1915, when the diabetic death-rate in the United States as a whole, and in Boston in particular, reached its height, being 17·5 per 100,000 in the United States and 26·1 in Boston, a fall in the diabetic death-rate has taken place, the figures for Boston for the years 1916–21 being 25·2, 19·1, 17·0, 22·9, 23·3, and 19·5. He points out that the decrease in diabetic mortality is by no means attributable to a lessened frequency of the disease, but is the result of better treatment. Between 1898 and 1913 the average duration of life of 940 fatal cases of diabetes in Boston was 3·3 years. In 1915 the duration of 113 fatal cases was 4·3 years, and for 1920 the average duration of 117 cases was 5·3 years. At the same time an increase in the incidence of glycosuria was shown by the fact that for 1,000 urines examined at the Metropolitan Life Insurance Company in 1919, 6 showed sugar, while in 1921 the ratio was nearly double, or 11 per 1,000, while in Joslin's private practice 50 out of 300 successive supposed non-diabetic patients, or 165 per 1,000, had glycosuria.

As the result of a questionnaire addressed to all the medical practitioners and hospitals in the canton of Basle, Hunziker, of the Basle Public Health Office, gained the following information: (1) At least 1 per 1,000 of the inhabitants of the canton of Basle were suffering from diabetes mellitus in the period between April 1, 1918, and April 1, 1919; (2) the disease was considerably more frequent in the later decennia than in early life, 152 of the 215 patients being over 50 years of age; (3) in Basle, as elsewhere, diabetes mellitus is more frequent in males than females; (4) the Jewish population of Basle shows a very high diabetes incidence; the proportion of cases among Jews and non-Jews being 15:1 among men, 7:1 among women, and 12:1 in both sexes.

Heiberg, of Copenhagen, has drawn up a table showing the duration of the disease in 1,503 fatal cases of diabetes, of whom 820 were males and 683 females, his figures being derived from the Danish Public Health Office and the statistics of the Medical Officer of Health for Copenhagen during a period of 10 years. The table shows that the duration of the disease is much longer when it commences later in life, and that it is longer in men than in women. The longer duration of the disease in men is to be attributed to their attention being drawn earlier to their condition in examination for life insurance.

Aetiology. Papers with statistical data relating to the aetiology of diabetes have recently been published by Mitchell from the Physiatric Institute under the direction of F. M. Allen, Sérégé, of Vichy, and Strauss, of Berlin. The predilection of the disease for the male sex is shown by the fact that of Mitchell's 116 cases, 70 were males and 46 females, and of Sérégé's 488 patients, 398 were males and 90 females. A definite history of diabetes in several members of the family was obtained in 46·6 per cent. of Mitchell's cases, and a history of diabetic heredity was present in 23 per cent. of Sérégé's series. Strauss, who found an hereditary history in 95, or 21·13 per cent., of 435 cases in soldiers observed between the beginning of the war and the autumn of 1916, remarks that this estimate approximates those of peace time, as given by von Noorden (18·5 per cent.), Schmitz (20 per cent.), Külz (21·6 per cent.), and Bouchard (25 per cent.). 65, or 56 per cent., of Mitchell's patients were Jews. Overeating was a probable cause in 33 per cent. of Sérégé's patients. Joslin (2) states that in one series of his patients a third acknowledged that they had eaten or drunk to excess, and in another series two-thirds admitted excess in food. Approximately 60 per cent. of Mitchell's patients were obese or gave a history of obesity. Alcoholism was incriminated in 9·2 per cent. of Sérégé's cases. 51, or 43·9 per cent., of Mitchell's series gave a history of a recent infection, such as influenza, gall-bladder infection, or gastro-intestinal disease. Syphilis figured in only 3 of his cases. Strauss, who obtained a history of recent infectious disease in 45 out of 125 cases of diabetes, emphasizes the fact that 30 were examples of infectious intestinal disorders such as dysentery, typhoid, paratyphoid, or cholera. On the other hand, a history of recent infectious disease was found in only 14, or 2·8 per cent., of Sérégé's cases, the diseases being appendicitis, influenza, and malaria. As regards the influence of wounds or other injuries, Strauss states that among 70 cases in which this cause could be assigned, in 90 per cent. the part affected was the chest, abdomen, or extremities, without the central nervous system being necessarily involved. In only five cases was there an injury to the skull, and in only two falls upon the head. Injury to the pancreas was noted in only one case.

Villaret and Blum, who record an illustrative case in a man aged 45, remark that the relations between diabetes and syphilis have been discussed for the last 50 years, two different opinions being held upon the subject. One school maintains that syphilis is a factor in diabetes by producing nervous lesions, while the other holds that syphilis is merely a debilitating agent without producing any localized lesion. Most of the cases of syphilitic diabetes on record have occurred in the tertiary stage. It is easy to understand how diabetes can be produced by a sclerotic, gummatous, or sclero-gummatous process affecting the liver, pancreas, hypophysis, or medulla, or by a meningeal process involving the nerve centres, medulla, or hypophysis. Cases of diabetes are much rarer in the secondary stage, though examples have been reported by Dub, of Prague, and Sewantie, of Paris. In the present case the diabetes appeared before the chancre had cicatrized, and the symptoms of diabetes developed side by side with those of the syphilitic infection.

Lemann, of New Orleans, points out that, though syphilis is extremely frequent in the negro, diabetes is less prevalent in the negro than among the whites, as is shown by the following statistics. During the years 1898–1909 the incidence of diabetes mellitus at the New Orleans Charity Hospital was 0·72 per 1,000 among the whites, and only 0·47 per 1,000 among the negroes. Similarly in the period 1909–19 the incidence of diabetes among the whites was 1·4, and among the negroes 0·85 per 1,000. Lemann concludes that there is no relation between the incidence of diabetes mellitus and syphilis, and probably no aetiologic connexion between the two.

A case suggesting a pituitary origin for diabetes mellitus is reported by Bleibtreu, of the Jena University Medical Clinic, in a woman aged 30, who presented enormous polyuria (19,500 c.cm. in the 24 hours) with a relatively small amount of sugar (456 gm.). A skiagram of the skull showed a remarkable deformity of the hypophysial region, neither the sella turcica nor the clinoid processes being recognizable. The nature of the changes was uncertain. Syphilis could be excluded by the history and negative Wassermann reaction, so that possibly a tumour was present in spite of the absence of all other symptoms. The case proved refractory to all the usual methods of treatment.

Symptomatology. Wilder classifies 298 patients with diabetes mellitus observed at the Mayo Clinic between January 1, 1920, and January 1, 1921, into the following 5 groups: (I) Acute diabetes, characterized by abrupt onset and gradually falling carbohydrate tolerance, strength, and weight. (II) Vascular diabetes, associated with hypertension or arteriosclerosis or both, with or without renal complications. (III) Diabetes of obesity, characterized by obesity without evidence of renal disease. (IV) Interstitial pancreatitis. (V) Miscellaneous persistent glycosurias. The aetiology of the first group, to which 57, or 19 per cent., belonged, was obscure. In only 10 was there a history of dietary excess. Physical exhaustion may have played a part in 4, and nervous exhaustion, worry, or anxiety in 4. In only 2 was there any suggestion of abdominal pain which may have been due to pancreatitis. 15 cases followed influenza. In 22 there was no evidence of any serious infection antedating the onset of the diabetes. In Group II the character of the disease was milder, and the course chronic. All the cases of diabetic retinitis observed during the year gave evidence of vascular disease. Gangrene occurred exclusively in this group, in which there were 80 patients, or 30 per cent. Group III contained 45 patients or 15 per cent. The diabetes in this group was of a mild type. The interstitial pancreatitis in the 53 patients who constituted Group IV was proved by operation, or suggested strongly by cholecystitis or other inflammatory conditions near the pancreas. The course of the disease was chronic in these cases.

Chalier, who records a case in a man aged 63, who had had diabetes for 8 years, emphasizes the importance of *adipsia* and pain in the epigastrium as premonitory signs of diabetic coma. Adipsia has not hitherto been mentioned as a prodromal sign of coma, whereas the significance of epigastric pain in this connexion has long been known.

From examination of the blood-pressure in 140 cases of diabetes, Rosenbloom (1), found that the *blood-pressure* in uncomplicated diabetes was normal or slightly below normal. In every one of the 22 cases in this series in which there was hypertension, nephritis, arteriosclerosis, or aortitis could be demonstrated. The presence or absence of sugar in the urine had no effect on the blood-pressure. Rosenbloom concludes that high blood-pressure in diabetes is due to chronic nephritis, arteriosclerosis, or cardiac hypertrophy.

According to Denecke, of the Greifswald Medical Clinic, who reports a case of *sudden death* in diabetes without coma or acidosis in a man aged 28, Frerichs has reported two similar cases, and von Noorden estimates that in 4 per cent. of all fatal cases of diabetes death is due to a cardiac cause. In most of these cases, however, death followed an intercurrent infectious disease, or resulted from arteriosclerosis, congenital weakness of the cardio-vascular system, or a persistent thymus, whereas in Denecke's case death was due to damage to the heart-muscle by diabetes, which is a very rare occurrence.

Gorke, assistant at the Breslau University Medical Clinic, reports a case of diabetes mellitus in a woman aged 57, complicated by *purpura haemorrhagica*, in which dietetic treatment was attended with an extraordinarily successful result.

Root, of the New England Deaconess Hospital, reports three cases of rare *paralysis* in diabetes. Two were examples of multiple neuritis complicated by chronic nephritis, and the third of isolated paralysis of the peroneal nerve not associated with the more frequent absence of reflexes and loss of sensation.

Rathery, Cambassédès, and Welti, who allude to the cases recently described by Labbé and Guillain (see *Medical Science*, 1921, **4**, 499), report a case of diabetic coma accompanied by *convulsive attacks* in a woman aged 45. The diabetes was of old standing, as its presence had been recognized for at least a year. The first symptom was violent headache, followed by vomiting, a fortnight later by aphasia, and then by an attack of Jacksonian epilepsy in another five days. The presence of acidosis was shown by a positive Gerhardt's reaction and the large quantity of acetone bodies and β-oxybutyric acid. Haemorrhagic pachymeningitis was found *post mortem*.

According to Pike, director of the State Hospital for the Insane at Darville, Pa., who records 3 illustrative cases, diabetes mellitus may occur in any *psychosis* as a purely physical complication, or, on the other hand, be a direct aetiological factor in the development of a psychosis. If it is recognized early and promptly treated, the progress of the mental disorder may be stayed. In these cases the intensity of the mental symptoms is in proportion to the toxaemia, and improvement of the sugar metabolism is marked by a corresponding improvement in the mental condition.

Rosenbloom (2) reports two cases in which the patients lost all their food tolerance with the onset of their *menstrual period*. One patient developed acute acidosis and died, although she was on a diet that had previously kept her sugar-free and free of acidosis. Rosenbloom attributes the loss of food tolerance to some temporary alteration in the function of the gonads, either an increased secretion or lack of correlation with the other endocrine organs.

Achard and Thiers report an example of diabetes in a woman associated with *hirsuties* of the masculine type, of which only a few previous cases have been recorded (see *Medical Science*, 1921, **4**, 502). The patient was a woman who developed hirsuties at the age of 9 or 10 and transient diabetes at 69. When death took place, two years later, the autopsy showed a fibromatous uterus, sclerosis of the ovaries, hyperplasia of the suprarenals, chronic thyroiditis with excessive colloid secretion, slight cirrhosis of the liver, and pericanalicular sclerosis of the pancreas. The writers regard the association of diabetes with hirsuties as a pluriglandular syndrome.

Hetényi, of the Third Medical Clinic of Buda Pesth University, examined 87 uncomplicated cases of diabetes and 14 with various complications such as degeneration of the myocardium, uncompensated cardiac disease, alcoholism, and hyperemesis gravidarum without finding a single case of *urobilinogenuria.* He comes to the conclusion that the liver in diabetes mellitus is in a condition of increased activity, inasmuch as it prevents the increased amount of urobilinogen, which under normal circumstances it could not deal with, from entering the blood-stream.

According to Terrien, the *ocular complications* of diabetes are frequent and various, being met with in more than 10 per cent. of the cases in the form of lesions of the cornea, iris, and choroid, cataract, retinal haemorrhages, changes in the optic nerve, amblyopia, affections of the vitreous, ocular palsies, and palpebral and orbital abscesses. In addition to these serious complications are certain ocular symptoms which though of much less gravity are of diagnostic value owing to their frequency and sudden development. Terrien classifies them under the heading of disturbances of refraction and accommodation. Changes in accommodation consist in presbyopia, which occurs at an unusually early age. Of 80 diabetic patients 11, or nearly 14 per cent., presented a diminution of the power of accommodation or, in more marked cases, actual paralysis of accommodation. The changes in refraction consist in hypermetropia, which may develop suddenly without any previous ocular disturbance or, on the other hand, in a transient myopia.

Hagen suggests that transitory hypermetropia is more common in diabetes than is generally supposed, and within 6 months he has seen this combination in 3 cases in his private practice. In every case the hypermetropia did not develop till a starvation diet had been prescribed for about a week, and the concentration of sugar in the urine had been greatly reduced. This hypermetropia persisted for a month and a half to two months, being demonstrable long after the glycosuria had ceased. After giving details of these 3 and 2 other hospital cases, Hagen concludes that this form of hypermetropia must be the result of antidiabetic treatment, and not a direct sequel to the disease itself.

The two questions which Mygind attempts to answer are: (1) Is *middle ear disease* common in diabetes, and (2) is the operation mortality high when mastoid disease is complicated by diabetes? His survey of the literature shows that opinions differ on both points, and he suggests that the writers who profess to be satisfied with their operation results have included in their statistics patients with simple glycosuria. As for the frequency of the combination, diabetes and acute middle ear suppuration, he finds it rare; among about 1,500 cases of acute middle ear disease treated at his hospital since 1905, he has seen only 6 with the above combination. The glycosuria in these 6 cases varied from 2 to 10 per cent., and all exhibited such characteristic symptoms of diabetes as hunger, thirst, emaciation, and polyuria. Only 1 of the 5 who underwent exploration of the mastoid process recovered. The remainder died of diabetic coma 1½ days to 2 months after the operation, which in every case was performed under ether anaesthesia. Mygind concludes that the coma was precipitated by the shock inflicted on the nervous system by the general anaesthetic, and he therefore recommends local anaesthesia and, if possible, delaying the operation till strict dieting has reduced the glycosuria. He would be tempted to advise against operative interference in such cases, were it not for the still worse prognosis involved in a passive attitude.

Mason states that in a series of 168 cases of diabetes mellitus treated at the Metabolism Clinic of the Royal Victoria Hospital, Montreal, 2 gave strongly positive *Wassermann reactions* in the blood, though there was no history or evidence of syphilis. In both cases the reaction became negative after slight antispecific treatment (two intravenous injections of neophenarsenyl), but there was a marked and rapid decline of the carbohydrate tolerance. Mason suggests that the arsenic acted as a toxic agent upon the weakened pancreatic cells, altering the quality or quantity of the internal secretion.

The subject of *diabetes in children* is discussed by Labbé (1), Lereboullet, and G. and J. Blechmann, of Paris, Mouriquand, of Lyons, Kochmann, of Berlin, Colburn, of Lincoln, Nebr., and Graham, of Melbourne. Labbé remarks that while diabetes in children does not differ fundamentally from that met with in adults it is practically only the severe form which is seen in children, whereas in the adult the bulk of the cases are moderate or mild and show no tendency to progress. Although diabetes is not frequent in children, Labbé has seen about 30 cases. Exceptionally it may occur during the first weeks of life, and its frequency increases with age. Kochmann, who reports a fatal case in an infant aged 4½ months, in whom death was preceded by staphylococcal folliculitis, broncho-pneumonia, and coma, states that the disease is extraordinarily rare during the first year of life, only six cases of the kind and none of them above criticism, having been collected by Stern. The diagnosis in Kochmann's case was based on the persistent excretion of glucose, and was confirmed by the autopsy, which showed a great deficiency of the islands of Langerhans and the presence of fatty changes in the liver and kidneys. According to Labbé, congenital syphilis is not of any greater importance in the pathogenesis of infantile diabetes than acquired syphilis in the aetiology of adult diabetes. Heredity appears to have more significance, although it is not frequent to find a diabetic patient producing a diabetic child, as in the case reported by Colburn in a child aged 22 months, whose father had had glycosuria for a number of years. In 3 of Labbé's patients the disease occurred in several members of the same family. The case described by Lereboullet and G. and J. Blechmann, a girl aged 9 who died after 5 weeks' illness, was also an example of familial infantile diabetes, her brother having died in diabetic coma after 9 months' illness at the age of 7. Labbé emphasizes the insidious character of the onset of diabetes in children. The child loses flesh and appears to be tired, the digestion is often defective and the general development is inadequate, often amounting to infantilism. Mouriquand remarks that polyuria is almost constant and is often the first symptom to attract attention. Polydipsia is another early sign which is rarely absent. Polyphagia, on the other hand, is less constant than polyuria or polydipsia, and is a late phenomenon. Pain in the epigastrium, in Mouriquand's experience, is commoner in the child than in the adult. On the other hand, boils, abscesses, and trophic lesions are less frequent in the child and usually only appear towards the end of the disease. The nervous system is also less frequently affected in the child, intense and obstinate headache being often the only symptom of this kind. As regards the prognosis, Mouriquand maintains that the diagnosis of diabetes in a child is practically equivalent to a sentence of death, and Kochmann maintains that the life of a diabetic child can be prolonged only for a few months even by the best treatment. On the other hand, Labbé (1), Joslin (2), and Graham are less pessimistic (see also *Medical Science*, 1920, **2**, 89).

Prognosis. Joslin (2) (3), states that the average duration of life in his fatal cases prior to June 1914, when undernutrition first began to exert its influence on his practice, was 4·8 years among 331 cases, whereas since June 1914 it has been 6 years among 597 cases. In the first decade, in which the disease is most severe, the duration has actually doubled, viz. from 1·2 to 2·7 years. A considerable number of fatal cases were of unusual duration. Thus 7 in the first decade lived beyond 5 years, 10 in the second decade beyond 6 years, 26 in the third and fourth decades beyond 10 years, 36 in the fifth and sixth decades beyond 15 years, which is within 6 years of the average expectation of life for their decades, and in the seventh decade there were actually 18 who reached or exceeded the average normal expectation of life for that period.

Rathery and Bordet found that the dosage of carbon dioxide in the alveolar air as determined by Joslin's modification of Fredericia's apparatus and technique gave very useful information as regards the acidosis of the patient. While in the normal individual the carbon dioxide tension varies from 38–45 mm. Hg, the writers found that in diabetes with slight acidosis it varied from 32–38 mm. Hg, in diabetes with moderate acidosis from 28–32 mm. Hg, and in diabetes with severe acidosis it was below 28 mm. Hg. They conclude that every patient with acidosis whose carbon dioxide tension is below 20 mm. Hg should be regarded as in a very grave condition. In coma the tension may fall to 10 or 5 mm. Hg. On the other hand, in every case of acidosis in which the carbon dioxide tension rises the prognosis should be regarded as favourable, at least for the time being.

Silvestri points out that the study of glycaemia in diabetes is of great importance, not only for diagnosis, but also for prognosis and treatment. Persistence of a high glycaemic concentration with a tendency to a gradual rise of the renal threshold while the patient is on a rational diabetic diet is a grave prognostic, and often indicates the occurrence of complications.

Treatment. Motzfeldt, of the Rikshospital, Christiania, has carried out the modern starvation treatment of diabetes, as advocated by American writers, during the past 3½ years, and has compared the results achieved in this period with those of the earlier period 1912–17, when such systematic dieting was not prescribed. In the first period there were 54 patients whose average age was 44. In the second period there were 77 patients whose average age was 36, and whose disease in many cases was severe. In the first series only 44 per cent. were discharged without glycosuria and ketonuria, in the second series 79 per cent. In the first series 24 per cent., in the second series only 9 per cent., were discharged with glycosuria and ketonuria. In the first series 13 per cent., and in the second series only 5 per cent., died in coma. Motzfeldt supplements these statistical data in favour of modern starvation treatment and total dietary restrictions with illustrative cases which show that even in childhood this treatment can restore to health cases of diabetes which a few years ago would have been regarded as inevitably and rapidly fatal. A valuable and simple clinical test in cases of acidosis threatened with coma is to note the time the patient can hold his breath. Although Motzfeldt's paper is largely confirmatory of Allen's system, he does not push dieting to such an extreme as Allen seems to find advisable.

In a discussion of the starvation treatment of diabetes Labbé (2) comes to the conclusion that in cases of diabetes without loss of nutrition this method can effect a rapid and complete cure, whereas in cases with loss of nutrition it yields only incomplete results and cannot restore the normal glycaemia. Even if the glycosuria and acidosis can be kept in check in some intermediate cases, the benefit obtained is only transitory, and the glycosuria and acidosis soon reappear. Labbé maintains that in diabetes with loss of nutrition starvation treatment should be reserved for the acute symptoms, such as the premonitory stage of coma and attacks of acidosis, and deprecates making these patients undergo repeated courses of starvation treatment.

Cammidge states that he has met with nervous disturbances in the form of ataxia and tetanic convulsions which necessitated the abandonment of the fasting treatment. A less serious complication observed by him was pronounced oedema.

The advantage of multiple meals in the treatment of severe diabetes is emphasized both by Gray and Murayama, of the New England Deaconess Hospital, who record illustrative cases. According to Gray the theory of divided meals appears to be activation of the liver by a small preliminary meal of carbohydrate, given 1 or 2 hours before each main meal; the organism being then in action at the time of that regular meal, responds to the food load more vigorously than with the schedule of three meals daily.

Orton, of the United States Department of Agriculture, who gives a list of vegetables with a low carbohydrate content, maintains that diabetics need a hobby to take their mind from their hunger trouble and give them an interest in life. This need is admirably filled by the culture of rare or uncommon vegetables. He points out that several of the vegetables suited for diabetic diets are beautiful plants, e. g. all forms of chard, chenopodium amaranticolor, and finocchio.

Joslin (2) maintains that coma is largely preventable and that the diabetic who dies of coma uncomplicated by infections dies needlessly. Only 1 per cent. of the cases at the New England Deaconess Hospital die of it, and it constitutes but one-third of the total deaths. As deaths from coma most commonly occur when the diet is suddenly changed, it is important that in severe, long-standing, complicated, obese, and elderly cases, as well as in all cases with acidosis, changes in the diet should be made gradually and not suddenly or radically. Joslin points out that gangrene comes next to coma as a preventable cause of death in diabetes. Injuries to the feet should not occur, as it is rare for diabetic gangrene to develop without any external trauma. Elevation of the foot, massage, quick douching with hot and cold water, will all promote re-establishment of the circulation and yield surprisingly good results. Many of the needless deaths due to diabetic gangrene were formerly connected with the anaesthetic, and Joslin is convinced that spinal anaesthesia or gas-oxygen has greatly lessened the mortality.

Bernheim, of the Surgical Clinic of the Hebrew Hospital, Baltimore, records three cases illustrating the importance of correlation between the physician and surgeon in the treatment of impending and actual diabetic gangrene.

Banting, Best, Collip, Campbell, and Fletcher, of the University of Toronto, have treated 7 cases of diabetes mellitus by subcutaneous injections of pancreatic extract (whole gland), and have come to the following conclusions: (1) Blood-sugar can be normally reduced even to the normal values; (2) glycosuria can be abolished; (3) the acetone bodies can be made to disappear from the urine; (4) the respiratory quotient shows evidence of increased utilization of carbohydrates; (5) a definite improvement was observed in the general condition of the patients, and in addition the patients themselves reported a sense of well-being and increased vigour for a period following the administration of these preparations.

Lhermitte and Fumet remark that about 10 years ago Herrick observed that removal of a small quantity of cerebrospinal fluid by lumbar puncture was sufficient to cause a very pronounced fall in the polyuria of diabetes insipidus. His observations were confirmed later by Graham, Williams and Rochester, Marañon and Guthierez, and the present writers, who now record two examples of diabetes mellitus in women aged 75 and 76, in whom removal of a small quantity of cerebrospinal fluid caused a considerable reduction in the quantity of urine excreted and in the amount of glycosuria. In the first case the polyuria dropped from 5 litres to 2 litres 700 c.cm., and the glucose from 188 gm. to 59·34 gm. in the 24 hours, and in the second case the glucose fell from 71·12 gm. to 0·72 gm. and the polyuria from 2 litres 500 c.cm. to 1 litre in 24 hours after the first lumbar puncture, while the results of the second puncture were equally striking, the polyuria falling from 3½ to 2½ litres and the glucose from 23·62 gm. to 4·50 gm. in the 24 hours.

Bickel, of the Geneva Medical Clinic, inspired by the work of Lhermitte and Fumet, measured the variations not only in the amount of urine and quantity of glycosuria, but also in the glycaemia following lumbar puncture. His patient was a woman, aged 73, suffering from diabetes, in whom lumbar puncture was followed by a fall in the urinary glucose from 83 to 38 gm. per 1,000 and by a fall in the morning glycaemia from 3·39 to 2·88 gm. per 1,000.

John, of the Physiatric Institute, Morristown, New Jersey, made a trial of eucalyptus infusion which had been recommended by Perez and Faulds in the treatment of diabetes, and found that it had no influence on the course of the disease. The observation is of interest in illustrating the fact that no drug has ever been found to possess any specific action on diabetes mellitus.

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MUMPS

Epidemiology. According to Sinclair, the incidence of mumps in the United States army in peace years was usually below 10 per 1,000 strength, but in war years the rates became excessive, especially in the Civil and World wars; the low rate of pre-war years increased in the war years 1917–18 to several times the normal rate, and in 1920 returned again to the normal rate of 10 in 1,000. An exactly similar rise occurred during the Civil War. During the three years 1917–19 there were 231,490 cases of mumps in the United States army, representing 6·5 per cent. of all diseases. In each 1,000 troops there were 2·5 constantly non-effective from mumps, this being 6·3 per cent. of the total non-effectiveness from all diseases. In other words, 3,540 men were constantly non-effective for three years from mumps alone. The incidence of mumps was thus exceeded in the late war only by that of influenza, these being two of the few diseases with higher rates in this than in other wars. A study of the distribution of mumps during the World War, according to native states, shows that the southern states had the highest rates, and the New England and eastern states the lowest, while the central and western states occupied intermediate positions. The average mumps rate in the French army in peace time is almost double that of the United States army, owing to the frequent increments of susceptible conscripts from rural districts. On the other hand, the English army peace time rate is very low, probably owing to the conditions of enlistment, which do not provide the same large increments of susceptible troops as in the French army, with its system of universal training. The conditions of life in army and naval garrisons, ships, and camps, and especially in war time, provide just what is necessary for transmission of the disease, viz. massing of susceptible material, and frequent direct and intimate contact of individuals, with the resultant epidemic proportions as soon as the virus is introduced. As regards season, mumps shows a distinct preference for the winter and spring months. In the United States army the highest rates for a period of ten years (peace time) were invariably in March and April and the lowest invariably in the autumn.

Symptoms. Friedjung remarks that while most German paediatrists, such as Baginsky, Bendix, Heubner, Kassowitz, Moro, and Widowitz, had not themselves observed more than one attack of mumps in the same individual, and mention only a few exceptional cases of repeated attacks reported by Hochsinger, Kalischer, and Schilling, French writers are inclined to regard recurrence of mumps as fairly frequent. Friedjung, who had previously recorded the case of a male infant, aged 15½ months, who developed acute swelling of the parotid four months after a typical attack of mumps, now describes a unique case of four attacks of parotitis in a child in the course of a year. The patient was a girl, aged 6½ years, whose second attack was barely five months after the first, the third three and a half months after the second, and the fourth nineteen days after the third. In the first attack the disease involved first the left and then the right side. In the subsequent attacks only the left side was affected. The first attack occurred during an epidemic of mumps, and the other three in a non-epidemic period.

According to Schwarzkopf, who records an example in a girl aged 11, localization of mumps in the submaxillary gland without involvement of the other salivary glands was first described by Leitzen in an epidemic at Halle in 1837, when in 6 out of 77 cases of mumps the submaxillary gland was affected exclusively. Panek, Spengler, and Löschner have recorded similar cases. Fehr also reported an epidemic of 16 cases of mumps, in 3 of which the submaxillary glands only were involved. Penzoldt described three cases which occurred in a small outbreak of mumps at Erlangen. The diagnosis was at first doubtful, as there had not been a previous case of epidemic parotitis. Typical cases of mumps, however, subsequently occurred showing that the cases with submaxillary gland involvement were due to the same virus. In Schwarzkopf's patient the condition was first mistaken for a haematoma and then for a glandular swelling of dental origin, and the diagnosis of submaxillary mumps, which was also suggested, was confirmed by the girl's mother developing typical epidemic parotitis.

At the Fifteenth French Congress of Medicine, held at Strasbourg in October 1921, Bénard, of Paris, read a paper on mumps orchitis, and testicular atrophy based on 400 personal cases of mumps, the statistics of various writers, and the statistics of the French army for the last 21 years, amounting in all to 200,000 cases. Criticizing the classical views relative to the frequency of orchitis, atrophy of the testicle, and impotence following mumps, he remarks that the frequency of simple orchitis in mumps, estimated by Laveran to be 33 per cent., is not really higher than 17 per cent. The proportion of bilateral to unilateral orchitis, estimated by some writers to be 20 bilateral to 100 unilateral, is reduced by him to 6 or 10 bilateral to 100 unilateral. In place of the classical figure of 66 per cent. of atrophies he substitutes 50 per cent. He points out that even in these cases the atrophy was always unilateral, almost always incomplete, often very slight, and, in a certain number of cases, transient, and liable to clear up entirely. As regards the development of impotence and feminism resulting from bilateral atrophy, a study of the literature shows that among about 180,000 cases of mumps there were only 5 certain and 5 possible cases—a proportion of 0·005 per cent., or one example in 20,000 cases of mumps. Bénard himself has always observed a persistence of genital aptitude, and even after double orchitis he has never found azoospermia.

Farnam, of the Yale University Department of Surgery, remarks that though there are 119 cases of *pancreatitis* following mumps on record, in only one instance, which was reported by Lemoine and Lepassat, was there an autopsy with objective evidence of the disease. In all the rest the diagnosis was based on more or less definite clinical signs. In 56 cases the number of days between the onset of the parotitis and the abdominal symptoms is given. In 28 the interval was 4–7 days; in 4 the time was 2 weeks; and in 10 the interval was less than 4 days.

In 5 patients, in whom the symptoms of pancreatitis were fairly well marked, the parotitis developed after the pancreatitis, in this respect resembling the orchitis which occasionally precedes mumps. The 119 cases included 4 in which the development of symptoms of pancreatitis was the only indication that the patient had mumps. All these 4 cases occurred in families which had recently had, or were having, mumps, and in persons who had not previously had the disease. Males appear to be more prone to the complication than females. Of 99 cases in which the sex is mentioned 81 were males and 18 females. This is partly due to the fact that many cases occurred in soldiers. The age incidence was also largely influenced by the same cause. The youngest patient was 11 months old and the oldest 58 years, but the next youngest was 4 years, and the next oldest 27. The complication may develop in mumps of all degrees of severity. In 12 other complications occurred, e.g. orchitis in 7, meningitis in 2, involvement of the submaxillary glands in 3, and of the sublingual glands in 1, and in 2 there were signs of meningitis. The duration of the abdominal symptoms is usually quite short. In a great many instances it lasted only 24–48 hours. The longest recorded is 25 days. All but the patient of Lemoine and Lepassat recovered. Farnam's case occurred in a man aged 23, in whom a mild attack of mumps was followed by abdominal symptoms diagnosed as acute pancreatitis. Operation showed a swollen, acutely inflamed pancreas with a large quantity of peritoneal exudate, from which *Streptococcus viridans* was isolated. Recovery took place without any sequelae. This is the only case on record in which pancreatitis associated with mumps has been seen at operation.

A case of *transient diabetes* following mumps is recorded by Labbé and Debré in a young man aged 18. Eighteen months after an attack of mumps, complicated by typical pancreatitis, the patient developed an erosion on the balano-preputial groove, which suggested the existence of glycaemia, and examination of the urine showed 4 gm. of glucose per litre. Reduction of the carbohydrates in the diet caused a very rapid disappearance of the glycaemia and the genital lesion, although impairment of the hepatic functions was shown by the presence of urobilinuria and slight acidosis. A comparison of this case with those reported by other writers such as Harris, Laignel-Lavastine, and Barbier suggests that mumps is capable of giving rise to an acute curable pancreatitis which is accompanied by transient insufficiency of the external secretion shown by digestive disturbance or by insufficiency of the internal secretion with disturbance of the regulation of sugar.

Pitres and Marchand report a case of *polyneuritis* in a soldier aged 20, in convalescence from a mild attack of mumps. The symptoms were violent pain, followed by paralysis and amyotrophy in all four limbs, loss of stereognosis and muscular sense, and abolition of the tendon, cutaneo-plantar, cremasteric, and abdominal reflexes. The paralysis diminished fairly rapidly, and some months after the onset inco-ordination was the principal feature. Mumps was the only infection that could be incriminated. The patient had never shown any evidence of syphilis or alcoholism. Three similar cases of polyneuritis of quadriplegic distribution following mumps have been reported by Joffroy (1886), Revilliod (1896), and Gallavardin (1898).

Toemann, whose observations are based on more than 1,200 cases of mumps in soldiers aged from 18 to nearly 50, has formulated the following laws relating to *mumps meningitis*: (1) Cytochemical meningitis revealed by changes in the cerebrospinal fluid is absolutely constant in mumps, and forms an integral part of the disease, the virus of which is eminently neurotropic. (2) The time of its appearance and disappearance varies considerably. Usually cytochemical meningitis is an early phenomenon, but sometimes it does not develop till late, on the occasion of some complication, such as orchitis, or without any apparent cause. It is usually fairly persistent, but sometimes it lasts only a short time. (3) Clinical meningitis, on the other hand, is by no means constant. In most cases it is entirely absent, and when present is almost always very slight. It sometimes appears very early, before any other sign of the disease, but as a rule it develops between the sixth and tenth day after the onset of the parotid swelling, and is almost always of short duration (3–5 days as a rule and 10 days at most). (4) Contrary to what is stated by some writers, clinical meningitis and cytochemical meningitis in mumps are absolutely independent of orchitis and of one another. A slight clinical syndrome is often associated with a very intense cytochemical meningitis, and, inversely, violent clinical symptoms are sometimes accompanied by only a moderate cytochemical reaction.

Urbantschitsch, of Vienna, records a case of mumps meningitis in a previously healthy man aged 23, remarkable first for the fact that symptoms of intoxication of both auditory nerves, consisting in tinnitus and deafness, preceded the parotid swelling, and secondly, for the contrast between the transient character of the mumps and the severity of the meningitis, which was manifested by intense headache, extreme tenderness of the cervical vertebrae and occiput, high tension, and increase of cells in the cerebrospinal fluid, with positive Nonne-Apelt and goldsol reactions. Apart from slight right-sided deafness, complete recovery took place.

According to Reverchon, Worms, and Delater, who report a fatal case of *oedema of the larynx* following an ordinary attack of mumps in a soldier aged 40, only a few similar cases have been recorded. Two fatal cases were reported by Courtille in his Paris thesis of 1828 and one by Jacob in 1875. Pilatte, in 1890, described a case where the patient's life was saved by tracheotomy. In spite of the apparent rarity of the condition, the writers are of opinion that the complication is more frequent than might be supposed, as they have observed three cases, including the present one, at the oto-rhino-laryngological clinic of the Val-de-Grâce Military Hospital in the course of six years. In the first two, however, the attack of laryngeal oedema was extremely mild. In all three cases the oedema was localized in the posterior part of the vestibule, and was secondary to a submaxillary localization of mumps. The anatomical conditions explain how the oedema, which readily develops in the cellular tissue of the inflamed submaxillary gland, spreads to the pharynx and larynx, whereas in the parotid it is shut in by a capsule which is closely adherent to the glandular parenchyma.

Treatment. The prophylactic and curative treatment of mumps orchitis by injection of diphtheria antitoxin introduced by Salvaneschi, and since advocated by Bonnamour and Bardin and other French writers on the supposition that it prevents the hyperleucocytosis of mumps and increases the number of red cells, is deprecated by Bénard and Carrieu, partly owing to the risks of anaphylaxis and partly owing to the extreme variability in the incidence of orchitis in different epidemics, which deprives the statistics published as to the efficacy of the method of much of their value.

The intramuscular injection of electrargol, followed half an hour later by 50 cgm. of aspirin, was found by Mallié to have a curative effect on mumps orchitis without having any of the drawbacks of diphtheria antitoxin.

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J. D. R.

DISEASES OF THE SKIN

Aetiology. Roberts, in an interesting article on the relation of certain chronic dermatoses to *focal infection*, gives details of 20 cases in which streptococci and staphylococci were found in the tonsillar crypts. From the results of his own observations and those of Barber on lupus erythematosus, he concludes that lupus erythematosus, lichen planus, prurigo, and alopecia areata are often associated with oral or tonsillar streptococci, and may recover after tonsillectomy, with or without treatment by auto-vaccines. On the other hand, psoriasis, although often associated with tonsillar streptococci, was not improved at all by tonsillectomy; neither was the status eczematicus. Discussing the relationship of oral infections to the cutaneous lesions, Roberts remarks that collections of bacteria in the tonsillar crypts occurring in normal individuals are not necessarily evidence of infection and must be distinguished from acute infection of the tonsils. The tonsillar crypts, he points out, are lined by keratinized epithelium, and the bacteria only gain access to the blood when this is ruptured. He mentions Vaughan's work on the non-specificity of the bacterial endotoxins, and remarks that this theory will explain the fact that widely different dermatoses such as lupus erythematosus, alopecia areata, lichen planus, and prurigo may be associated with the same tonsillar bacteria; and, vice versa, the same end result may be connected with different bacteria. He points out that there is no evidence that these dermatoses are due to direct streptococcal infection of the skin. More probably they and other chronic skin diseases are due to defence reactions provoked by the entrance of foreign proteins into the blood, the chief portal of entry being the surface lymphoid tissue. Thus, removal of the tonsils arrests the supply of foreign proteins produced by streptococci and other bacteria in the tonsillar crypts, which cause 'subinfection' of the lymphoid tissue. Under these conditions, as Roberts remarks, the effect of vaccines must be regarded as doubtful, and it is noteworthy that in his cases of lichen and prurigo improvement took place before the vaccines were given.

Nicolas, Massia, and Dupasquier discuss the aetiology of *pellagra* and report five cases in subjects who were badly nourished but did not eat maize. According to these observers, the maize theory as the specific cause is exploded; nevertheless, maize may give rise to pellagra when it is the only article of diet, owing to its deficient nutritive value. The true cause they consider to be hypo-alimentation, qualitative or quantitative, aggravated by bad hygiene, mental depression, or alcohol. The sole use of a single foodstuff such as maize may therefore cause pellagra; in one case a diet of eggs was the cause. They remark that there is no clinical distinction between true pellagra and pseudo-pellagra, and suggest the term 'pellagroid syndrome' to include both.

Winfield considers that most cases of true *ano-genital pruritus* are of infective origin. In 50 cases he found *B. coli* in 40 and *Streptococcus faecalis* in 30, in the exudate, and obtained improvement by using a vaccine prepared from cultures of these organisms.

Some interesting work has been done on the *infectivity of herpes* by Blanc and Caminopetros, Levaditi, Harvier and Nicolau, and others. The first-mentioned observers found that the contents of the vesicles of herpes labialis and herpes genitalis, when inoculated in the cornea of rabbits, gave rise to keratitis, which was sometimes followed by fatal encephalitis, and when inoculated subdurally also caused encephalitis. Inoculation of the cornea with cerebral matter from rabbits which died of this herpetic encephalitis reproduced keratitis. These results were not produced by the contents of the vesicles of herpes zoster. Levaditi found that cutaneous inoculation of rabbits with the virus of epidemic encephalitis caused a papulo-squamous dermatitis containing the same virus, which, when reinoculated, caused fatal encephalitis. According to Levaditi and his collaborators, herpes and epidemic encephalitis are caused by variants of the same ultramicroscopic virus, which has an elective affinity for the ectodermic tissues—skin, cornea, and nervous system—the virus of herpes being more dermotropic than the others.

Worms and Lavergne discuss the association of *herpes zoster with facial paralysis.* They regard herpes zoster as of infective origin, and attribute the facial paralysis sometimes associated with it to infection of the geniculate ganglion, which presses on the motor fibres in the bony canal. They hold that the geniculate ganglion represents the posterior root ganglion of the sensory branch of the facial nerve (nerve of Wrisberg), and that the herpetic eruption follows the course of this nerve, which is distributed to the anterior two-thirds of the tongue, part of the tonsillar region, the external auditory meatus, and parts of the concha. As this nerve also supplies the internal and middle ear, the attack of herpes may be associated with deafness, tinnitus, and vertigo. Details are given of five cases. The authors conclude that herpetic infection is one of the causes of facial paralysis, and that such cases can be diagnosed by the appearance of vesicles on the external auditory meatus and on the tongue and fauces. These cases must not be mistaken for acute otitis media with facial paralysis.

Bruusgaard has investigated the occurrence of *haematogenous infection in trichophytia.* He points out that cases of trichophytia profunda, or kerion celsi, are often accompanied by acute exanthemata and general symptoms such as fever, swelling of the glands, spleen, and joints. The usual exanthem resembles lichen scrofulosorum (lichen trichophyticus); sometimes it is morbilliform or scarlatiniform, and occasionally it resembles erythema nodosum. These secondary eruptions appear at the height of the reaction, when immune bodies are most abundant; hence, they may be connected with the phenomenon of allergy and of haematogenous origin. Bruusgaard describes a case of severe kerion in a woman aged 68, involving the submental and submaxillary regions and accompanied by a general papulo-pustular secondary eruption and severe general symptoms. A trichophyton identical with that of the primary lesion on the chin (*T. gypsicum*) was cultured from the lesions of the secondary eruption (on maltose and glucose agar) and spores were found microscopically. He remarks, however, that these secondary eruptions are not all haematogenous; some may be caused by the fungus spreading directly from the primary focus.

In answer to the question: Is *erythema nodosum* infectious? Andersen refers to a family consisting of a mother, aged 45, and five children living at home. In November 1921 she developed erythema nodosum, and the rash was still present when, on December 12, her son, aged 13 years, developed the disease. The same disease broke out on the 15th in a son of 8, and on the 16th in a son of 22. In the case of the mother and the eldest son the illness began with a sore throat.

Holland, of the skin department of the Rikshospital in Christiania, quotes his chief, Professor Bruusgaard, as writing in 1914 that no case of erythema nodosum, clinically diagnosed as such, has yet been traced to the tubercle bacillus by microscopic examination, inoculation of animals, or tuberculin tests. Holland adds that this verdict is as true to-day as it was in 1914. Two cases have, indeed, been recorded (Laederich and Landouzy and Gutmann), in each of which a single tubercle bacillus has been demonstrated in the lesion, but its presence there may well have been accidental, not causal. Between November 1916 and December 1921, 13 cases of erythema nodosum were treated at the Rikshospital. In 9 cases, 8 of which were recent, inoculation tests were made, but none of the 13 inoculated guinea-pigs developed tuberculosis. One of the patients was a woman with lupus which, on inoculation into a guinea-pig, promptly gave a positive result. Another patient was a woman, aged 27, who suffered simultaneously from typical erythema nodosum and erythema multiforme. This combination is not rare, and if erythema nodosum is tuberculous, why not also erythema multiforme? Yet the fashion of including skin eruptions of obscure origin among the tuberculids has certainly not yet extended to this disease. Early in 1922 a workman, aged 19, developed erythema nodosum of the legs, and redness and swelling of the right tonsil. There was no family history of tuberculosis, but the hilum shadows were enlarged, and Pirquet's reaction was positive. Inoculation of two guinea-pigs with fresh nodes proved negative, but cultural tests yielded, after 48 hours, a short, Gram-positive, anaërobic streptococcus.

Discussing the relation of lupus erythematosus to tuberculosis, Sundt records the case of a girl of 10, who suffered from lupus erythematosus during the last five years of life. Death followed an attack of erysipelas with abscess formation. There was no history of contact with any tuberculous person, and the necropsy showed no evidence of tuberculosis. Even the microscopic examination of the bronchial and mesenteric glands failed to disclose tuberculosis, and though Pirquet's reaction was said to have been positive at one time, Sundt doubts the correctness of the interpretation of the cutaneous test and is inclined to regard this case as a proof that the origin of lupus erythematosus is not necessarily or invariably due to the tubercle bacillus.

Symptomatology. In the Section on Dermatology at the last annual meeting of the British Medical Association, O'Donovan opened a discussion on *occupational dermatitis.* His personal observations included 2 cases of hyperkeratosis due to friction, one in a painter from the constant use of a scraper in the right hand, the other in a boot-repairer from handling a short hammer; 4 cases of carcinoma due to friction, one in a baker who developed a warty growth on the thumb of the right hand from the use of a hot poker, one to the irritation of an embedded wedding-ring, one of cancer of the tongue in a boot-repairer, due to irritation by nails held in the mouth, one in a taxi-driver who developed cancer in a patch of lupus on the left wrist from irritation caused by the driving wheel. In the last two cases syphilis and tuberculosis, respectively, were predisposing causes. As regards dermatitis due to dirt, O'Donovan mentions two cases in which dermatitis was caused by mending old and dirty sacks. Occupations involving constant immersion of the hands in water are more liable to cause dermatitis, e.g. fishmongers' assistants. He has observed occupational dermatitis in dental mechanics from the handling of plaster of Paris, benzene, and acids for cleaning metal plates ; also, from handling naphtha, in a girl who painted golf balls. As regards the food industry, he mentions a case of papular dermatitis in a labourer who unloaded barley; bullous dermatitis in pea-pickers, due to irritation from the 'May weed'; baker's itch and sugar itch, and a case of dermatitis due to handling figs, on the surface of which a parasite was found. Preservatives, such as formalin and sulphurous acid, may cause dermatitis. Concerning oil dermatitis, he points out that the chief cause of irritation is the presence of minute steel or other gritty particles in the oil. He mentions two cases of occupational tinea, one in a barber affecting the nails, the other in a labourer who unloaded hides. Concerning tar epithelioma, he points out its slow development (after 10 to 40 years' exposure), its low malignancy, the regional lymphatic glands being seldom involved, and its response to treatment by radium. In conclusion, O'Donovan remarks that occupational dermatitis depends largely on individual susceptibility, also on skill in avoiding contact. There is little or no specificity in the skin reactions, and erythema, pustulation, perionychia, and carcinoma may all be due to various industrial causes.

Legge classifies the causes of industrial *dermatitis* as follows : (1) chemical substances, such as potassium bichromate, arsenious acid, and certain dyes; (2) substances which soften and macerate the skin, such as alkalis; (3) substances which dissolve and remove the natural grease from the skin, such as turpentine and benzene; (4) processes which mechanically injure the continuity of the skin, such as scratching. Preventive measures which he recommends include the application of an ointment of lanoline and castor-oil after work.

Roberts regards occupational dermatitis as due to two causes, a defect in the keratin membrane of the skin, and the personal idiosyncrasy of the patient, which he considers chemical in nature. The introduction of foreign proteins into the body from septic foci reduces the resistance of the skin. Also foreign carbohydrates which do not enter into the normal sugar metabolism may sensitize the skin to certain irritants. Hence the diet may play a part in the preventive treatment of dermatitis.

Lancashire classifies *dermatitis artefacta* in four groups, excluding cases of malingering. The first group includes hysterical subjects who mutilate themselves with the object of exciting pity or gaining notoriety. The second group includes subjects who mutilate themselves with no apparent object. Some of these are cases for the alienist. The third group is similar to the second, but differs in the absence of self-satisfaction. These cases are examples of uncontrollable impulse or obsession. The fourth class includes subjects who cause skin eruptions through simple habit, similar to nail-biting. The diagnosis of dermatitis artefacta may be easy or difficult, according to the skill of the subject. The main points concern the history of the case, the distribution and character of the lesions, and especially their uniformity. Suggestion to the patient of a new site for the next eruption is sometimes of assistance. In some cases mild irritants, such as eau-de-Cologne, will produce severe eruptions, probably depending on psychic predisposition.

Thibierge (1) (2) discusses the transmission of *animal itch* to man. The sarcoptes of the cat is smaller than that of man, and the female does not lay the eggs in burrows. The eruption following contagion from the cat is papulo-vesicular, resembling that of other parasitic contagions, but characterized by a symmetrical grouping of the papules on the regions which have been exposed to contact, and by the absence of burrows. The eruption following contagion from the dog is similar in nature and also occurs on exposed parts. Veterinary surgeons and those who come much in contact with horses are liable to contract horse-itch, the forearms being the parts usually affected.

Dermanyssus gallinae may also produce an eruption of the forearms in those who tend fowls infected with this parasite. An eruption similar to that described above has been noted in dock labourers engaged in discharging grain from Russia, Roumania, or Africa, caused by a small acarus (*Pediculoides ventricosus*). Contagion from animal itch is usually direct, but may be indirect from the animal resting on clothing or in beds. Treatment is simple, and consists in baths and sedative ointments, such as zinc ointment containing 5 per cent. ichthyol and 1 per cent. menthol. Strong parasiticidal ointments, such as sulphur, are unnecessary, as the sarcoptes soon dies on the human skin.

Rivalier reports a case of *tinea tonsurans* in an adult woman aged 30. The lesions were diffuse, and were caused by the small-spored endothrix.

Thibierge and Legrain have investigated three cases of *foetal ichthyosis.* They found no evidence of hereditary or familial incidence. In one case there was evidence of syphilis in the mother, and in another case probable syphilis in the father. In two of the cases there were congenital malformations of the eyelids and ears. They conclude that heredo-syphilis is the chief cause of this condition.

Sabouraud states that *trichorrhexis nodosa*, *trichoclasia*, and *trichoptilosis* are in the great majority of cases not due to disease of the hair but to trauma caused by strongly alkaline shampoo powders, dyes, and the processes of curling and waving the hair. Spontaneous trichorrhexis of the moustache and patchy trichoclasia of the hair without perceptible lesion of the skin is sometimes observed, but is rare and of unknown aetiology.

Queyrat reports a case of *vitiligo* in a girl aged 13, who suffered from severe nervous shock owing to a shell from 'big Bertha' dropping into the church at which she was at mass. A fortnight later blanching of the hair occurred in patches together with symmetrical patches of vitiligo on the body. Queyrat mentions two other cases of vitiligo following shock reported by Darier and Leloir, in which the intervals were 8 or 10 days and 3 or 4 weeks respectively. In both these cases there was trauma, but this was absent in his case. Inquiry into the family history and examination of the girl showed some evidence of heredo-syphilis, which he thinks was a predisposing cause.

Fraser describes a *favoid scalp affection*, known as 'wit-kop', prevalent among the syphilitic natives of Bechuanaland. This affection is not met with in Europeans, or in non-syphilitic natives. The evidence suggests that 'wit-kop' is a special papulo-pustular syphilide, although in cases of long duration a fungus of the Achorion type has been isolated. The affection responds readily to treatment by arsenobenzene and mercury.

Tomkinson reports the instance of a family in which the mother and six children were affected with *alopecia areata* and *strabismus*. Microscopic examination of the affected hairs was negative. The Wassermann reaction was not tested. Tomkinson thinks that these cases lend support to the nervous origin of some forms of alopecia areata.

Low draws attention to the frequent *association of eye-lesions with rosacea*. As most of such cases consult the ophthalmologist first they are seldom seen by the dermatologist. The eye-lesions are: (1) a mild palpebral conjunctivitis; (2) a more severe ocular conjunctivitis with small grey papules surrounded by dilated capillaries, resembling phlyctenular conjunctivitis; (3) keratitis, which may proceed to ulceration and result in corneal opacities. According to Low, the eye-lesions correspond to the cutaneous lesions; the mild conjunctivitis to the areas of dilated capillaries of rosacea; the phlyctenular lesions to the papules of rosacea; the ulcerative keratitis to pustular rosacea. Another eye-lesion possibly connected with rosacea is chalazion.

Feldman describes a case of *conjugal lichen planus*. The lesions were of similar distribution in husband and wife, both on the skin and mucous membrane of the mouth. Both were in good health and not related by blood. The affection appeared in the wife eight months later than in the husband. Feldman suggests the possibility of an infective origin.

Butler reports two cases of *erythema multiforme* confined to the mucous membrane of the buccal cavity. The lesions consisted of denuded areas covered with a greyish secretion and the remains of ruptured vesicles. The diagnosis was confirmed by the subsequent appearance of typical lesions on the dorsal surface of the hands in one case, and by a history of such lesions in the other case.

Goodman finds that *non-syphilitic ulcers of the leg* are twice as common in the left leg. In a series of cases ulcers of the left leg gave 73 per cent. negative Wassermann reactions, while ulcers of the right leg gave 40 per cent. He attributes the greater frequency of simple ulcer of the left leg to static conditions depending on the anatomical differences between the left and right iliac vessels.

Parounagian and Goodman report a case of *granuloma inguinale* occurring in a syphilitic patient. The lesions, consisting of foul, ulcerating nodules, affected the groins and perianal region, and also the upper lip and neck. There was a history of a venereal sore six years previously, and the tongue was affected with syphilitic glossitis. Injections of silver-salvarsan and neo-salvarsan caused little or no improvement, but the Wassermann reaction became positive. Microscopic examination of the lesions was negative for new growth, tubercle, and syphilis, but Donovan bodies were found, both intra- and extra-cellular. The authors point out the rarity of lesions of the lip in this condition.

Beeson mentions a case under the care of Terra, of Rio de Janeiro, with lesions of the lower lip. This case was cured by intravenous injections of tartar emetic.

Warfield reports a case of *sporotrichosis* in a negro in which a metastatic nodule was found in the upper lobe of the right lung after death, but none in the other viscera. The patient during life presented multiple nodules on the face and limbs. There were also pulmonary symptoms and a radiogram showed a shadow in the region of the hilum of the right lung. The sporothrix was cultured from the nodules. Treatment with potassium iodide and arsenobenzol failed.

Treatment. Bareat reviews the results of *radium treatment* in various dermatoses. In *angioma planum*, or port-wine stain, inflammatory reaction should be avoided. Four or five sittings at intervals of 2 or 3 months are necessary to produce discoloration. Radiferous plaques containing $\frac{1}{8}$ mgm. per cubic centimetre, moulded on the surface and surrounded by lead protective, may be applied for 3 to 5 hours. Treatment of these cases is always difficult and liable to result in unequal discoloration and telangiectases. *Angiomatous tumours* are more easy to deal with. They may be treated by the ultra-penetrating method, avoiding ulcerative reaction, at three-month intervals, or by insertion of needles containing 5 mgm. of radium.

In *lupus*, isolated nodules may be treated by the total method applied for 7 hours; more extensive patches by the penetrating rays for 24 hours; 1, 2, or 3 applications at intervals of 3 months. Parts already cicatrized are protected by lead and gutta-percha to avoid telangiectases. Nasal lupus may be treated through aluminium tubes. *Lupus erythematosus*, is only suitable for radium in fixed cases, and the results are doubtful.

In *cheloid*, radium treatment may be combined with scarification; or the scar left after excision may be treated by radium.

In *leukoplasia*, radium treatment gives inconstant results. Radium is often beneficial in *senile keratosis*, *warts*, *papillomas*, and *corns*; the last require ultra-penetrating rays; flat juvenile warts small doses by the ordinary method.

In *lichen planus* the usual method may be used for the lesions, and the ultra-penetrating rays applied to the nerve-roots. *Psoriasis* and *mycosis fungoides* react to radium, but the progress of disease is not arrested.

Radium may also be used in ointments containing 15 per cent. radium bromide solution (1 mgm. per litre) in localized pruritus and eczema. Radioactive water is said to be useful in some cases, as a sedative to the nervous system and as an eliminator of uric acid.

Dubois-Roquebert reports good immediate results with radium in 16 cases of cancer of the lip, mostly inoperable cases or post-operative relapses. A vulcanite splint carrying tubes of radium or radium emanations, fixed at 10 mm. distance from the surface of the lesion was applied to the lip. When the growth was more than 20 mm. thick, radium puncture was employed by platinum needles containing radium or radium emanations.

In the Annual Report of the Manchester Radium Institute, Burrows states that there were 36 permanent cures out of 71 cases of *rodent ulcer*; that 25 per cent. of cases of carcinoma of the lip remained well for over 2 years, and about the same percentage of cases of carcinoma of the skin for 2 to 7 years; that 50 per cent. of cases of cavernous naevus were cured without leaving a mark; that keloid and scars almost always yield to radium treatment, and that a good proportion of lupus cases, if not too far advanced, can also be cured.

In the Annual Report of the London Radium Institute, Pinch states that cure or improvement was obtained as a rule in cures of chronic eczema, seborrhoeic eczema, lichenification, cavernous naevi, keloid, papillomata, keratomata, corns, rodent ulcer, lymphosarcoma, and sarcoma of the nasopharynx. In the case of the malignant lesions the term cure is modified to arrested development. Improvement was obtained in psoriasis, xanthelasma, xeroderma pigmentosum, leukoplakia, capillary naevus, lupus erythematosus and lupus vulgaris, tubercular adenitis, cicatrices, and epithelioma of the skin. The results were doubtful in cases of pruritus and in epithelioma of the buccal cavity.

Lortat-Jacob (1) (2) points out that the direct application of *carbonic acid snow* is open to several objections. In the first place it does not attain the optimum temperature of −80° C. owing to the fact that a layer of carbonic acid gas intervenes between the snow and the lesion; secondly, it is not sterile. To obviate these drawbacks Bordas invented the cryocautery, which consists of a double tube, with a vacuum between the outer and inner tube, containing a freezing mixture of carbonic acid snow with acetone, alcohol, or ether. Béclère drew attention to the importance of regulating pressure as well as temperature and invented an apparatus by which pressure could be registered. Lortat-Jacob describes his own modification, in which the snow is produced directly in the apparatus, and which also has a device for registering pressure. The amount of pressure to be used varies with different lesions, but is seldom more than 1,500 gm., and the time of application generally under 40 seconds. The action of the snow cannot be bactericidal, because it has been shown that the tubercle bacillus and other organisms will survive at extremely low temperatures. According to Lortat-Jacob, the action is one of cellular necrosis at the point of application, with ischaemia and thrombosis in the deeper tissues. He has found that lupus erythematosus and senile facial epithelioma are most suitable lesions for this form of treatment, and that it also gives good results in most forms of naevus, acne rosacea, sycosis, palmar keratosis, some cases of warts and corns, chloasma, lentigo, xanthoma, tattoo-marks, radio-dermatitis, and cheloid. In horny and hyperkeratotic lesions a more powerful action is required, and this may be attained by adding more acetone. The chief advantage of carbonic acid snow treatment, when properly performed, is the aesthetic cicatrix produced.

The method of *auto-haemotherapy*, introduced by Ravaut in 1913, has been applied by Nicolas, Gaté, and Dupasquier to several dermatoses. The best results were obtained in pruriginous dermatoses due to diathesis, of which prurigo is the type. Benefit was also obtained in some cases of eczema, urticaria, and neuro-dermatitis with lichenification, but none in lichen planus. The authors believe that the action of auto-haemotherapy depends on modification of the soil, 'a disturbance of the colloidal equilibrium', manifested by haemoclasic crisis. In lichen planus, which, they say, resembles an eruptive disease more than one due to diathesis, the soil is less concerned; hence the failure of auto-haemotherapy. The signs of haemoclasia observed were leucopenia and lowered tension, and in some cases severe reactions with rise of temperature, arthralgia, and swelling of the joints.

Heiberg and With have investigated the effect of *general carbon arc-light baths* in the treatment of *lupus* at the Finsen Institute, Copenhagen. It had already been shown by Reyn that the addition of general light baths, especially the carbon arc-light, to the usual Finsen method increased the percentage of cures from 60 to 90. Heiberg and With find that the carbon arc-light by itself will cure lupus, but that the cure is hastened by the simultaneous local application of the Finsen light.

Jacobson claims favourable results in lupus with intramuscular injections of *benzyl-cinnamic ether*, a method which he had previously found successful in pulmonary tuberculosis. A course consisted of 12 daily injections, 5 of 1 c.cm., 5 of 1·5 c.cm., and 2 of 2 c.cm. Three courses were given with intervals of two weeks, and repeated after a month's interval. In 30 cases of lupus treated in this way suppuration subsided, ulcers healed, and tuberculous nodules underwent cicatrization.

Zeisler recommends the application of *acid nitrate of mercury* solution as a rapid and effective method, especially after preliminary X-ray treatment. Prolonged X-ray treatment of lupus is liable to be followed by epithelioma in the cicatrices, and radium treatment by atrophy and telangiectases.

Harmer also recommends general carbon arc-light baths combined with direct irradiation of local foci in cases of *lupus of the buccal cavity*. In the case of the larynx the rays are applied through a speculum.

Ravaut reports a severe case of *trichophytic sycosis* cured by *intravenous injections of Gram's solution*, after failure of the usual forms of treatment. In 3 weeks 10 injections were given, commencing with 1 c.cm. diluted with 5 c.cm. of water, and progressively increased to 5 c.cm. diluted with 15 c.cm. of water. There was slight local reaction with the larger doses, but no general reaction. When seen 6 weeks later the case remained healed and was negative microscopically.

Ravaut and Boulin also report a case of *kerion*, due to trichophytic sycosis, which was cured in a fortnight by *intravenous injections of Lugol's solution*. The sycosis was contracted from a horse, and treatment was commenced 20 days after onset. Daily injections were given, commencing with 1 c.cm. and increasing to 5 c.cm., diluted with 20 c.cm. of normal saline.

Lutembacher reports favourable results from *intravenous injections of salicylate of sodium* in an obstinate case of generalized *psoriasis*. Injections were given daily, commencing with 1 cgm. and increasing to 3 cgm. dissolved in 80 c.cm. of distilled water.

Goubeau relates his further experience with *carbon tetrachloride*, which he has used successfully for several years in cases of acne, psoriasis, mycosis, &c. This drug, which causes deep disinfection of the skin, Goubeau finds useful in ordinary seborrhoea and in severe seborrhoeic eczema. It is first applied in anhydrous lanoline, afterwards undiluted.

Scholtz and Richter have tried the effect of *intravenous injection of grape sugar* on the skin. According to these observers, sugar favours the passage of fluid from the skin to the blood-vessels, and has a beneficial influence on eczema and also on toxic erythemas. They found that when potassium iodide ointment was applied to the skin the drug was excreted in the urine in 2 to 4 hours after an intravenous injection of grape sugar; otherwise very little was excreted. The dose of sugar injected was from 8 to 15 gm. given in a 25 to 50 per cent. solution.

Feldman and Ochs recommend *permanganate of potassium* solution (1 in 5,000 to 1 in 1,000) as a local application in the treatment of eczematoid ringworm and tinea circinata.

Gutierrez reports good results from intravenous injections of *neoarsphenamine* in *yaws*. In 275 cases a clinical cure was obtained in 94 per cent., after one or two injections of 0·6 gm.

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C. F. M.
C. L.

ABSTRACTS

SURGERY

Piney, A. Carcinoma of the bone marrow. *Brit. J. Surg.*, 1922, **10,** 235.

When the conception of a 'cancerous diathesis' was no longer tenable, pathologists turned to the blood- and lymph-channels as the means of conveyance of metastases. Emboli of cancer cells were soon demonstrated in the lymphatics, but it remained for Sampson Handley to show the importance of 'lymphatic permeation', or actual growth of cancer cells, along the lymph-channels from the primary focus outwards.

At birth, all the bones except the cranial, contain red marrow in which there is no fatty tissue. In the adult, red marrow alone still occupies the vertebrae, sternum, ossa innominata, and the greater part of each rib. In the long bones of the limbs the only red marrow to be found is in a small area at the upper ends of the diaphyses. Even in adult life, however, this red marrow can increase in amount in response to various stimuli—e. g. in leukaemia. The minute blood-channels of the fatty marrow (best demonstrated in specimens which have been injected with a carmine-gelatin mass) are ordinary, well-formed vessels. The red marrow, on the other hand, is essentially a tissue consisting of innumerable blood-channels with extremely thin walls, outside which are haematopoietic cells. At the junction of the red with the fatty marrow there is a great widening of the stream-bed, which must cause a corresponding decrease in the rate of flow. The veins in the medullary cavity possess no valves.

The lining cells produce red cells on the side towards the lumen, white cells on the other side. This explains the ordinary hyperplasia of the red marrow, for under no conditions is there an increase of the leucoblastic tissue without a concomitant increase of the erythroblastic. The converse is also true. Neither can any injury of one tissue leave the other intact.

As to lymphatic channels in the bone-marrow, it has frequently been stated that these are absent, but the proofs have not been forthcoming. From the author's own investigations, also, the only statement possible at present is that modern methods of injection have not demonstrated the existence of any structures in the bone-marrow which resemble lymphatics in structure or in distribution.

Almost every case of cancer shows some degree of anaemia, but not of a specific character. When, however, the marrow has been invaded by metastases the blood picture so closely resembles that of pernicious anaemia that, when first observed, the anaemia was supposed to be primary and the malignant growth merely incidental. The alterations in the blood are independent of the site of the primary growth and are only related to the presence of metastases in the marrow. As in pernicious anaemia, there is a reduction in the number of red cells, a high colour-index, anisocytosis with presence of nucleated red cells, both normoblasts and megaloblasts. On the other hand, there is slight leucocytosis instead of the slight leucopenia common in pernicious anaemia, while there is a relative increase of the neutrophil polymorphs as contrasted with the relative lymphocytosis of the latter condition. In a word, there is grave disturbance of the erythropoietic organs with a certain amount of stimulation of the leucopoietic mechanism. It is admitted that cases of carcinosis of the marrow are on record in which there was no such blood picture as the above, and a possible explanation is suggested.

The author quotes four cases of bony metastases studied minutely by him, and points to the position of the cancer cells in channels lined by endothelium and containing red blood corpuscles, to the escape of the distal bones of the limbs from involvement, to the absence of evidence of the permeation of fascial lymphatics in the neighbourhood of the invaded bones, to the position of the metastases, which is always in the red cellular marrow and not first in the periosteum, and to the points of emergence of the tumour on the surface of the bones, which correspond to the places of exit of the veins.

Previous observers, following von Recklinghausen, had championed the theory of the spread of metastases to the bone-marrow by way of the blood-stream, but in recent years the work of Sampson Handley has influenced opinion in the other direction. Piney contends that, as far as bone metastases are concerned, the inferences which Handley has drawn from his admittedly accurate observations do not necessarily follow from them.

It may be objected that cancer cells could not be carried to the marrow without involvement of the lungs. It has been shown, however, that small thrombi containing cancer cells are common in the capillaries of the lungs even when there is no tumour in these organs visible on ordinary examination. Cells may thus easily pass through the lesser circulation to the greater and yet lodge in the red bone-marrow where the stream-bed of the blood widens, the course of the vessels becomes more complicated, and the conditions for the lodgement of an embolus become correspondingly more favourable. Piney's definite finding of carcinoma cells inside blood-containing vessels is a valuable piece of evidence.

C. C. E.

Masci, B. Sarcomi multipli primitivi delle ossa. [**Multiple primary sarcomata of bones.**] *Policlin.*, 1922, **30**, Sez. Chir., 473.

This article is a contribution to the vexed question of multiple 'myelomata'—to the condition, that is to say, characterized by severe pains with multiple nodular tumours in bones, particularly those of the head and trunk, without deposits in any other tissues, and often accompanied by albumosuria. Of the 93 published cases collected by Hirschfeld in 1910, many of the records were incomplete, a few related to endotheliomata, lymphadenomata, lymphosarcomata, or true sarcomata, but most of them were central myelomata or chloromata.

The author's case was that of a man of 59 who was an alcoholic and chronic bronchitic, but otherwise strong and healthy. In the course of four or five months no less than 30 tumours appeared on the ribs, clavicle, mandible, and frontal bone, accompanied after a time by severe pains, secondary anaemia, and cachexia; there was never any evidence of involvement of any other tissue; spontaneous fracture occurred. In the ribs the tumour seemed to be definitely medullary, but that on the clavicle rather periosteal in site, and the frontal mass, which was removed, penetrated the bone and reached the dura. Repeated examinations failed to reveal albumose in the urine. The growth was made up of masses of round cells of equal size, with large nucleus and very scanty cytoplasm; the stroma was minimal; there were no fusiform cells or myeloplaxes or epithelioids; the growth was extremely vascular.

Albumosuria is not present in all such cases; there was none in those recorded by Scheele, Herxheimer, Collin, or Devic and Bériel, and it is sometimes intermittent. Whilst the anaemia is usually secondary only, the blood picture is inconstant; there may be normoblasts or myelocytes, and the leucocyte formula is sometimes 'inverted'. The medulla may be so widely invaded as materially to affect the amount of haemopoietic substance, so that normoblasts and megaloblasts appear, together with red cells of bizarre shapes with kariokinetic figures; there may be neutrophil myelocytes or lymphoid medullary cells. The variety of primary multiple tumours of bone is considerable, and it is becoming increasingly difficult to make a diagnosis on clinical or macroscopic evidence. For some authors 'myelomata' are tumours composed of masses of large cells with big nucleus and abundant non-granular protoplasm, but without myeloplaxes or giant cells, without fusiform or lymphoid cells; some look upon the cells as myelocytes of embryonic type; some admit the presence of myelocytes, myeloblasts, or erythroblasts, but exclude cases in which immature cells appear in the blood, or those with leukaemia, whilst admitting the green-coloured tumours as 'chloromyeloma'. The term 'myelosarcoma' applies to the cases in which tumours of myeloid cells are found in extra-medullary organs.

In some multiple tumours there are plasma cells with simulation of lymphoid tissue; multiple sarcomata proper have less uniformity of cell type; endotheliomata have their cells in direct relation to vessel walls, the cells tend to cubical or cylindrical shape and their arrangement simulates adenomatous structure; these tumours grow very slowly, are discretely limited, and have a high glycogen content. Chloroma occurs in children in the bones of the face and cranium, and is characterized by extensive periosteal infiltration, as well as by the colour; sometimes there is grave anaemia, the whole haemopoietic system is involved—spleen, liver, and lymphatic glands—and the picture may be one of acute lymphatic leukaemia.

The writer's own case appeared to be a small round-celled sarcoma without any of the variability of cell-type usual in multiple sarcomata; he is able to find seven similar cases in the literature, and thinks it undesirable that the term 'myeloma' should be extended to cover tumours with similar histology, whilst admitting that distinction is sometimes difficult. At the same time, cases of round-celled sarcoma, strictly limited to the bones, and perhaps to the bones of the skull and trunk only, should be considered as a separate systemic disease. E. R. C.

Barrie, G. Haemorrhagic osteomyelitis. *J. Bone & Joint Surg.*, 1922, New Ser. **4**, 653.

Under this caption Barrie describes a condition said to be often erroneously diagnosed and treated as malignant. Both the author's description and the comments of those who heard the original paper leave one in doubt as to whether it is anything more than myeloid sarcoma or perhaps fibrocystic disease of bone masquerading under a new name.

Most common in the young, the condition generally affects the lower limb, particularly the femur. In 75 per cent. of the cases a history of injury can be elicited. Contrary to what one might infer from the name employed, it is not an acute inflammation but a gradual thickening in either the shaft or one extremity of the affected bone; tender, but only slightly painful. The bone is expanded and the X-ray shows rarefaction, but the periosteum is never broken through. Microscopically the growth is seen to be identical with granulation tissue. Giant cells are found, but differ from those of neoplastic origin. Bacteria have never been isolated from the removed tissue. There are no evidences of malignancy, and all the cases finally recover after curetting, neither amputation nor resection being ever required. C. C. E.

Stewart, M. J. The histogenesis of myeloid sarcoma. *Lancet*, 1922, ii, 1106.

The views of Barrie (*vide supra*) and of other American writers on 'haemorrhagic osteomyelitis' are traversed by Professor Stewart. Clinically and pathologically, myeloid sarcoma is a sharply defined entity. Its histogenesis is, however, most obscure. Stewart regards bone as an intimate association of two tissues: (1) the osteoblastic and osseous tissue proper, from which osteosarcoma arises; and (2) the specialized fibrous tissue framework, which not only encloses and supports the bony tissue proper, but also provides the multinucleated osteoclasts. Myeloid sarcoma he regards as a specific tumour taking origin from this fibrous tissue framework. Of the two elements of the tumour, the polymorphous cell-tissue is almost certainly fibroblastic in nature, while the 'myeloid' giant cells are merely altered osteoclasts. The differences between these cells and osteoclasts (increased size, increased number of nuclei, &c.) are only such as are commonly associated with neoplasia. They are an integral and essential part of the tumour, not needing to be accounted for by the presence of some foreign substance, exogenous or endogenous.

On this view 'osteoclast sarcoma' would be the obvious name for the tumour, but until its true nature and histogenesis have been fully elucidated it would be better to adhere to the name 'myeloid sarcoma', introduced nearly 70 years ago by Sir James Paget, than to invent other names, above all such a one as 'haemorrhagic osteomyelitis'. The growth is undoubtedly neoplastic, albeit of only local malignancy, in the great majority of cases. Cases are quoted in which there was recurrence even after resection of the involved bone. Mere curettage is futile, and it is mischievous to teach that all that is required is 'the removal of unhealthy and excessive granulation tissue and inflammatory débris'.

There can be little doubt that two classes of cases, essentially distinct, are being grouped together by American writers on the subject.

C. C. E.

Fairbank, H. A. T. Late results of treatment of congenital dislocation of the hip. *Brit. J. Surg.*, 1922, **10**, 24.

The writer reviews all the cases treated by him between the years 1903 to 1914; the number quoted is 146, with a total of 175 joints.

The method of reduction was the Lorenz method, modified in so far that stretching of the adductors was employed instead of rupture. The position after reduction was flexion and abduction to a right angle, with plaster to the knee, and patients were encouraged to walk after a month. In the majority of unilateral cases the plaster was removed after six months and no further treatment employed.

A simple classification is given of the after results. In *Class I* are those cases where the head of the femur is in the acetabulum and approaches the normal in size and shape. *Class II* includes cases in which the head is in the acetabulum, but in which the head and neck are either mushroomed, varoid, or partly absorbed ('absorptive arthritis'). *Anterior reposition I* contains cases in which a well-formed head is opposite the upper lip of the acetabulum with or without a socket; *Anterior reposition II*, cases in which there are gross bony changes, usually marked absorption of the head, and flattening of the bone at the site of the upper lip of the acetabulum.

Percentage results are worked out in age groups for the unilateral cases: under 3 years = 70 per cent. cures; 3 years to 5 years = 41 per cent.; 6 years and over = 28·5 per cent., the percentage of anterior repositions increasing with the increase in age. In the bilateral cases cures under 3 years = 46·6 per cent.; 3 years to 5 years = 22·7 per cent.; 6 years and over = 33·3 per cent. The apparent discrepancy in the proportion of cures of bilateral cases in patients over 6 years of age is explained by the fact that all bilateral cases over 6 were done, whereas in the unilateral cases a great number over 6 years were rejected. This percentage table brings out the importance of early diagnosis.

In the imperfect results some additional cures may be obtained by a second manipulation, followed by open operation in which an upper lip is made for the acetabulum, without opening the joint.

It would appear that a great number of anterior repositions are followed by considerable arthritis, and the late after-results of this particular type are not regarded by Fairbank so optimistically as by some other authorities.

J. B. H.

Evans, E. Laming. Late results of manipulation treatment of congenital dislocation of the hip. *Brit. J. Surg.*, 1922, **10**, 15.

In this article the writer has collected 49 cases of congenital hip seen between the years 1903 and 1916, and analyses 31 cases involving 38 joints, that he has been able to follow up. He considers that the old anatomical classification of results leaves much to be desired, and suggests a fuller one.

Group I. Concentric reduction with normal head and neck. In this group, which is considered the standard to be aimed at, he places 26 per cent. of his cases.

Group II. Concentric reduction with changes in head and neck. These changes are diverse in character, the commonest being diminution of the angle of inclination, buffer-shaped head, spreading of the head over the neck, and absorption of the neck. In this group he places 34 per cent. of cases.

Group III. Excentric nearthrosis. In this group are cases showing changes in the acetabulum, usually absorption of the upper part, so that the head has formed a new joint at a higher level, and changes in the head and neck usually accompany this excentric reduction.

Group IV. Anterior transposition. The writer states that in this group there are few changes in the head and neck; this probably accounts for the good functional result obtained.

Group V. Posterior redislocation. These are similar to the untreated cases except that changes in the length and direction of the neck are frequently found.

Group VI. Loss of head and neck. This is not a common sequel of the treatment, the writer having only one case in which the end result was functionally a fair one.

Group VII. Unreduced dislocation. In all his cases the method of reduction employed was founded on Lorenz's technique, modified considerably by the gradual change from a disruptive to a more gentle process.

The after-treatment has been encasement in a short spica down to above the knee, with early locomotion on a high patten. The period of retention for unilateral cases has been from a year to eighteen months, the attitude maintained being one of 90° flexion, 70° abduction, and indifferent rotation. In the bilateral cases the retention has been shortened as much as possible, usually to three to six months. J. B. H.

LOVETT, ROBERT W. The diagnosis and treatment of some common injuries of the shoulder-joint. *Surg. Gynec. & Obst.*, 1922, **34**, 437–44.

The shoulder-joint in the quadruped is a weight-bearing joint, but in man, in the upright position, it is called upon to support the weight of the arm—perhaps 10 or 15 pounds—and is a purely hanging joint. This weight is supported by the muscles, not by the capsule. The relation of the surrounding muscles to the joint structures is most intimate and most important. Of the bursae the most important is the subdeltoid or subacromial, which lies on the greater tuberosity of the humerus and the tendons of the rotators with its roof attached to the acromion and the acromio-clavicular ligament. It is of about the size of a silver dollar and does not, as a rule, communicate with the joint. Owing to the strength of the pectoralis major and the latissimus dorsi, the total effect of muscular balance is to favour an adducted position of the arm.

The classical and too familiar picture is that in which, from over-use, a wrench, exposure to cold, or perhaps some slight systemic infection, the shoulder becomes painful, and abduction and rotation are limited. There is little tendency to spontaneous improvement, and atrophy of the shoulder and arm muscles ensues. Where many of the joint structures are involved it is impossible to make an accurate anatomical diagnosis. The terms 'sprain' when acute, and 'periarthritis' when chronic, may be retained, but such stock diagnoses as 'neuritis', 'torn ligament', and 'subdeltoid bursitis' should be avoided.

A sprain may be due to a stretching or tearing of capsule or ligaments, to injury of the synovial membrane, or to extravasation of blood into the tendon-sheaths or other structures. Muscular strain most commonly affects the deltoid, the biceps, or the internal rotators. If any fibres are torn there will be acute pain on pressure over the spot and on attempts at voluntary contraction. There will be a certain amount of haemorrhage and, if the muscle is superficial, a prominence may be detected at the site of rupture when the muscle is put into action. Acute synovitis is less frequent in a typical form in the shoulder than in, for example, the knee, as the capsule plays so small a part in the support of the arm and in the limitation of arm movements.

Rupture of the supraspinatus tendon occurs from a fall or from severe exertion, as in golf. Attempts at abduction are futile and are excessively painful. If the tendon itself is ruptured wholly or in part the diagnosis may not be clear, but more often a piece of bone is detached from its insertion and is readily shown by the X-ray. Subdeltoid bursitis undoubtedly does occur, but is much less common than is usually supposed, and is sometimes merely secondary to joint involvement.

The two essential requirements in the treatment of acute cases are that the weight must be taken off the capsule and supporting muscles and that the pull of the two strong adductors must be antagonized. The use of a sling in any but slight cases is to be deprecated. The only efficient means is a platform splint of wire, plaster of Paris, or other material which holds the arm at a right angle to the long axis of the body with the elbow flexed at a right angle and the forearm horizontal. When the acute stage is over it is useful to employ light massage followed by active exercises. Where adhesions have already formed, with the arm in adduction and inward rotation, massage is not tolerated. The arm should be fixed and supported as much away from the side as possible, gradually increasing the degree of abduction as the irritability quiets down. Later on, gentle passive stretching may be cautiously employed and, still later, manipulation under anaesthesia.

Operation will be required in true chronic bursitis of the subdeltoid bursa which has not yielded to milder measures; also in those cases where the insertion of the supraspinatus has been torn away, and where, after placing the arm in an abduction splint, the X-ray shows that the bony fragment is still not in place. The operation of Sir Robert Jones is described in detail.

Irritable arm—false neuritis. These are the cases in which symptoms out of all proportion to the cause follow over-use or slight injury of the shoulder-joint. There is no true neuritis. The arm feels heavy and aches after use. Abduction becomes limited and the muscles atrophy. Treatment consists in the use of a sling, the gentlest possible massage, radiant heat, and exercises to develop the muscles. The severest cases will require an abduction splint and the stretching of adhesions.

The author does not refer to ionization. C. C. E.

Linell, E. A. On solitary fibromyxomata of peripheral nerve-trunks, with a description of a case of cystic fibromyxoma of the median nerve. *Brit. J. Surg.*, 1922, **10**, 202.

Linell's case was that of a woman of 42, on whose right arm, just above the elbow on the mesial aspect, a painless rounded swelling had been growing for four years. Beyond occasional shooting pain radiating from the mass down into the middle finger there were no symptoms of any kind, and no disability. The tumour was fusiform, of the size of a pigeon's egg, not attached to the skin, and freely movable from side to side, but not in the long axis of the limb. It was painless to touch and elastic in consistence, but not fluctuating. At operation, it was found to be blue in colour and cystic, dark fluid blood escaping on incision. In view of its possible malignancy, the median nerve was resected above and below the tumour, and end-to-end suture performed. The fibres of the nerve could be seen spread out on the surface of the tumour. On microscopic examination, the cyst wall was found to consist of a loose network of branching cells, with areas of myxomatous degeneration and of well-developed fibrous tissue. The nerve was free from infiltration above and below the mass, which was therefore diagnosed as a cystic fibromyxoma.

The only two similar cases which the author has found recorded are both described in Alexis Thomson's monograph on neuroma and neurofibromatosis (1900). F. M. R. W.

McGuire, E. R., and Burden, J. F. Unusual case of sarcoma of the median nerve. *Surg. Gynec. & Obst.*, 1922, 453.

McGuire and Burden's case was that of a woman of 40, who for the preceding five years had been aware of the presence of a small painless mass on the anterior aspect of the right forearm. Five weeks before admission to hospital, an increasing swelling of the forearm in the region of the mass had occurred, associated with severe pain in forearm and hand. The authors state that 'there was slight diminution of function over distribution of medial nerve, but not sufficient to be noticed by the patient'. Operation revealed an elongated mass apparently connected with the median nerve. Nine inches of the nerve together with the mass were resected. Subsequent examination showed it to be 15 cm. in length by 4·5 cm. in diameter. It was firm in consistence and pinkish in colour, and appeared to have invaded the sheath of the nerve. Microscopic examination gave a typical picture of neurofibroma at the distal pole, but at higher levels rapidly growing fusiform cells and cells of irregular outline showing mitotic figures were seen. There were also giant cells and numerous dilated capillaries. The nerve-fibre bundles were separated by growth and were atrophic. The diagnosis of spindle-celled sarcoma originating in a neurofibroma was made. Recurrence at the seat of operation occurred within a few weeks and amputation above the elbow was performed. Previously, radium and X-ray treatment had been tried without benefit.

Neurosarcoma appears to be of rare occurrence, and the authors could find only two similar cases in the literature of the past few years. These are briefly described. F. M. R. W.

Frazier, C. H. Trigeminal neuralgia. A surgical approach to the spheno-palatine ganglion. *Ann. Surg.*, 1921, **74,** 328–30.

In this well-illustrated article Frazier describes an operation devised by himself and his assistant, Dr. Francis C. Grant, for the purpose of exposing and extirpating the sphenopalatine ganglion for those cases similar to trigeminal neuralgia, but held by some (e. g. Sluder) to be referable to the sphenopalatine ganglion.

He agrees that there are neuralgias of the face that are not attributable to the trigeminal nerve and that they can be relieved by cocainization of the sphenopalatine ganglion. He speculates that in these cases the pain may be associated with the sympathetic connexions of the ganglion.

Attempts at alcoholic injection of this ganglion are very likely to fail; it is small and inaccessible. The only way to prove the existence of these sphenopalatine neuralgias of Sluder and to treat them, if they definitely exist, is to remove the ganglion. Access is gained by traversing first the zygomatic and then the sphenomaxillary fossa. The steps of the operation, which he has performed in two cases, are well demonstrated by the illustrations to the article.

1. The incision has a straight limb along the zygoma; from the anterior end of this one curved limb extends up to and along the supra-orbital ridge; and another, also curved, runs down the infra-orbital ridge.

2. The malar bone is exposed and cut with a Gigli saw in three places, (1) through the frontal process, (2) through the maxillary process, and (3) through the zygomatic process. To make sections (1) and (2) the Gigli saw is entered through the sphenomaxillary fissure. The zygomatic process is only partly sawn through and then fractured outwards so as to hinge on its outer periosteum. On turning the malar bone backwards the zygomatic fossa is laid open.

3. The pterygoid plate is exposed, by displacing backwards the areolar tissue and the temporal muscle and by detaching the internal pterygoid muscle.

4. Part of the pterygoid plate is removed and the sphenomaxillary fossa exposed. The maxillary division of the V nerve is found as it enters the orbit through the sphenomaxillary fissure and is followed up to the ganglion; this is not otherwise readily found, as it is far back and surrounded by fat. There is little haemorrhage; the internal maxillary artery is not seen; only its branch, the infra-orbital artery.

An excellent view is obtained by using the illuminated retractor that Frazier employs in his Gasserian ganglion operations. C. C. C.

Woltman, Henry W. Malignant tumours of the nasopharynx with involvement of the nervous system. *Arch. Neurol. & Psychiat.*, 1922, **8**, 412–29.

Woltman draws attention to the fact that many cases of malignant disease of the nasopharynx are wrongly diagnosed in their early stages because pharyngeal symptoms are not then prominent, whereas extra-pharyngeal symptoms are common and particularly attract attention. Thus in 16 of 25 cases pharyngeal symptoms were absent. Early manifestations include pain in the face or in the side of the head, headache, deafness, tinnitus, diplopia, blindness, proptosis, facial paraesthesia, cervical adenopathy, dysphagia, aphonia, hoarseness, and distant malignant metastases.

Out of 79 cases of malignant nasopharyngeal tumour seen at the Mayo Clinic 25 showed involvement of the nervous system. The cranial nerves were usually caught in their extracranial courses; the nerves passing through the orbit, particularly the sixth, were those most commonly involved. Next in order came the trigeminal nerve; 11 of the 25 patients had sensory changes, and 6 motor paralyses, referable to this nerve.

The author emphasizes the need of thorough nasopharyngeal examination early in a case presenting unexplained cranial nerve palsy, unexplained cervical glandular enlargement, or symptoms suggestive of the presence of pituitary tumour or of tumour of the Gasserian ganglion.

He gives a table showing the errors of diagnosis and treatment made in the 25 cases, and another illustrating the frequency of involvement of the different nerves. C. C. C.

Mennell, Z. Anaesthesia in intracranial surgery. *Proc. Roy. Soc. Med.*, 1922, **15** (Sect. of Anaesth.), 13–18.

Owing to the comparatively small flow of blood though the brain when the intracranial pressure is much raised, a higher percentage of anaesthetic in the blood is necessary in order to secure anaesthesia than when the intracranial tension is normal. Directly the pressure is relieved by the opening of the dura, an enormous increase at once takes place in the volume of blood flowing through the brain, anaesthesia becomes deeper, and a dangerous dose of anaesthetic may suddenly bathe the medullary centres. The brain is singularly tolerant of changes of pressure provided that they are induced gradually, but sudden variations in pressure constitute by far the most important factor during operations for cerebral tumour.

There are other special circumstances connected with these cases. The surgeon may require the patient to be prone, or semi-prone, with extreme flexion of the neck, or to have the head propped up vertically ; the face may be covered with towels, thus interfering with a free airway ; a mechanical airway will be useless if the anaesthesia must be kept too light for one to be tolerated. To meet all these difficulties, intratracheal ether is the method *par excellence.* The aim should be to give the minimal dose compatible with efficiency. Any change in the strength of the vapour must be extremely gradual. To avoid vomiting, which leads to protrusion of the brain and to venous haemorrhage, one hand is always kept on the jaw and when any attempt at swallowing is felt (the precursor of vomiting) the strength of the ether is slightly increased. In cases in which the frontal sinus is opened, the blood and irrigating fluid are liable to collect in the nasopharynx and will give trouble unless an intratracheal catheter is being used.

A sudden fall of blood-pressure may be inevitable from opening the dura, from loss of blood or from the removal of a tumour. This is to be combated by gentle pressure on the brain and by giving less anaesthetic. Stimulating drugs are regarded as of no value at this stage, but after the flap has been replaced large doses of camphor are sometimes given. When a tumour is to be removed from the cerebellum or from the lateral recess, direct disturbance of the medullary centres may cause such a fall of blood-pressure that the radial pulse may be impalpable for twenty minutes. With care, however, the patients usually recover quickly and show no bad effects. Mennell himself does not use the corneal reflex in estimating the depth of anaesthesia. Those who do should remember that a diminished or absent corneal reflex on one side may constitute one of the symptoms of the lesion for which the operation is being done. C. C. C.

Sourasky, A. On errors of refraction in hyperthyroidism. *Lancet*, 1922, ii, 611.

The fact that exophthalmos is so frequently associated with hyperthyroidism would lead one to infer that errors of refraction were not infrequent in this condition. Sourasky points out that the general belief is that there are no such refractive changes. He therefore examined 20 cases of hyperthyroidism, 16 of whom had exophthalmos of varying degrees. Of the 32 eyes every one showed some abnormality : hypermetropia 1 ; hypermetropic astigmatism—simple 1, compound 13 ; myopia 2 ; myopic astigmatism—simple 7, compound 5 ; mixed astigmatism 3. It is seen, therefore, that of 32, 29 showed astigmatism, but it is interesting to note that the axis of the astigmatism does not follow a certain course, as would be expected if it were due to pressure of the lids upon the protruding eyeball. Furthermore, it was present in 7 cases where there was no exophthalmos.

He comes, therefore, to the conclusion that although hyperthyroidism causes astigmatism one cannot yet say whether this eye change is a general manifestation or is caused by the changed local conditions.

He points out that the headaches, which so frequently occur with this disease, disappeared when the astigmatism was corrected, and the history of the headaches corresponded closely with the history of the disease.

A. J. W.

Forni, G. Contributo allo studio dello scleroma della laringe e della trachea. [**Contribution to the study of scleroma of the larynx and trachea.**] *Arch. ital. di chir.*, 1922, **6**, **1**.

In 1882 Frisch demonstrated the constant association of a bacillus with scleroma, but its specificity, for rhinoscleroma, is not universally admitted, since the bacillus is not always found in the diseased tissues and is sometimes found in the healthy nose or in simple rhinitis, and since other organisms are sometimes found in the lesions. Histologically, characteristic tissue changes are found, with peculiar cell types named after Russell, Mikulicz, and Pellizzari. Hebra's original ascription of the name 'rhinoscleroma' was soon found inadequate, for the extent of the parts liable to involvement merits the title 'scleroma respiratorium' given by Wolkowitsch. In 1886, 84 per cent. of the recorded cases showed nasal localization, but, in 1910, Pachonski's 273 cases showed the larynx affected in 223; nasopharynx 172; nose 155; pharynx 67; trachea 75; and bronchi 12 times. Mikulicz stated that the morbid process began in the mucosa or submucosa as an infiltration with small cells, of which some became epithelioid and some were transformed into spherical bodies with hyaline contents. Later appeared exuberant granulations or small nodules projecting from the surface into the air-passages, accompanied or followed by the development of a deforming or stenosing cicatricial tissue. Others describe an initial stage of chronic catarrh and desquamation, and regard this condition as favouring the entry of bacteria from the surface. Certainly, if the specific bacillus enter with inspired air, it might be expected that the nose and mouth would be first and most often attacked, but this is not the case. The author's own observations suggest an initial phase, not necessarily specific, of dry catarrh and desquamation, and he regards individual predisposition as no more than the expression of such an antecedent condition, which likewise determines the site of the scleromal lesion in the respiratory tract. Contagion seems to be extremely rare even where the disease is common, as in Galicia. Onset is commonly between the ages of 20 and 30; sex seems to have no influence; but poverty, hardship, and exposure figure frequently in the anamnesis. Experimental reproduction has practically always failed.

The initial stages have rarely been examined, even in the larynx, because they are painless and the patients usually present themselves only when obstinate cough, or hoarseness, or dyspnoea have supervened, as the cords or the infraglottal region, respectively, are involved.

In the larynx the infiltration may be diffuse, or polypose and scattered.

The nodular form predominates in the parts above the glottis, but the other type also occurs and results in severe cicatricial stenosis or occlusion. The epiglottis, the pharyngo-glottic and glosso-epiglottic folds may be involved. The cords themselves, which are long resistant, may show small nodules, or be involved diffusely by extension from below, the infraglottal region being most often primarily attacked. The whole laryngeal aperture may be transformed into a cone, or appear as a small orifice in a fibrous membrane; the arytenoid cartilages may be immobile. In the trachea the nodular type of infiltration is more frequent and the posterior part is more generally attacked. Here, the danger of suffocation arises not only from actual stenosis, but also from the difficulty of evacuating viscid catarrhal products.

Of the author's three cases, one was a healthy man of 28 years, who in 1910 had for two years had difficulty with respiration and some pain in the throat, choking sensation when swallowing, and a hoarse voice. For three weeks he had been much worse. The condition was thought to be due to papillomata, but a tracheotomy showed stenosis of the trachea which was treated by dilatation and a cannula was worn for four months. In 1915 he returned to the clinic, having had recurrent and increasing trouble for about a year. He then had a laryngo-fissure and further dilatation. In 1921 a very rapid and severe return of dyspnoea resulted in death, despite a low tracheotomy and deep intubation. The larynx and trachea were so extensively infiltrated that their normal contours were obliterated. Histological examination revealed the usual features, here described at length and well figured. The author was unable to confirm the theory of the production of the Mikulicz cells by the intracellular multiplication of the bacilli.

The other two cases recorded had similar histories, but both were eventually subjected to deep irradiation with substantial benefit; 'cure' the author regards as so far very exceptional. The duration of the disease may be very prolonged—in one of his cases 27 years—and the serious symptoms arise not from intoxication but from mechanical interference with respiration or from intercurrent pulmonary maladies. Autovaccines have hitherto given no results. Laryngo-fissure is generally necessary, perhaps more than once, and may be associated with extensive sharp-spooning of the trachea, a procedure fortunately not attended with much bleeding. Salts of radium may be used in the trachea and bronchi. The long tracheal canula is badly borne. E. R. C.

Wilkie, D. P. D., and **Hartley, J. N. T.** **Pharyngeal diverticula and its surgical treatment, with a record of two cases.** *Brit. J. Surg.*, 1922, **10**, 81–93.

The authors give a *résumé* of the literature of pharyngeal diverticula and show that the condition was first described by Sir Charles Bell, who pointed out that the pouch was of pharyngeal origin and that the explanation of its occurrence was the presence of sphincter action at the lower part of the pharynx.

They give an account of its aetiology, clinical manifestation, and diagnosis. It occurs most frequently in men past middle life and is more common than it has hitherto been supposed. Two factors produce the condition: the one, weakness of the wall, and the other increased intrapharyngeal pressure brought about by inco-ordinate action between the propulsive and sphincteric elements of the pharyngeal muscle.

In the matter of diagnosis radiographic methods have replaced all others. When treating the condition they lay stress on two points: one, the dilating of the lower part of the pharynx and the other removal of the sac. In removing the sac the ideal way is the one-stage operation, but owing to the danger of cervical sepsis they advocate the two-stage operation. In this they employ a modification of the usual procedure by removing only the mucous sac and stitching the cut edges over a bougie passed into the oesophagus to ensure that the pharynx is not unduly narrowed. They claim by this method the risk of cervical sepsis is very greatly lessened.

J. B. H.

Arzela, I. Contributo anatomo-patologico e clinico allo studio delle cisti linfatiche del grande epiploon. [**Contribution to the pathological anatomy and clinical study of lymphatic cysts of the great omentum.**] *Policlin.*, 1922, **30**, Sez. Chir., 417.

Cysts of many different origins are met with in the mesentery and omentum. The classifications of Dowd, Niosi, and Brunetti, may be superseded by a more comprehensive one which may be tabulated thus:

- Congenital cysts
  - simple
    - serous
    - chylous
  - neoplastic
    - ectodermal (epidermoid)
    - mesodermal
      - lymphatic
        - lymphangiomous
        - chylangiomous
      - Wolffiian
    - endodermal (enteroid)
    - teratomata and foetal inclusions

(any of the above may be complicated by intracystic haemorrhage).

- Acquired cysts
  - encapsuled haematomata
  - parasitic
  - gaseous.

In the present article the author is concerned with the simple serous variety and recounts a case occurring in a healthy male of three years. Prominence of the belly had been noticed since the first year of life, but, though steadily increasing in size, had given rise to no symptoms until quite recently, when frequency of micturition had appeared. The child was thin and pallid, but, apart from the abdomen, otherwise normal. The belly was distended by a large fluid swelling which moved as a whole with changes of posture; no fever, no eosinophilia, no cuti-reaction. The cyst, which contained a litre and a half of clear lemon-coloured fluid, was pedunculated and attached in the upper part of the mid-line of the epiploon; there were no adhesions.

The cyst-wall, about 1·5 to 4 mm. thick, had three layers; the inner was of formed fibrous tissue with scattered groups of endothelial cells; the middle layer was loose reticular connective tissue, with some fibromyoma cells, lymphatics, and lymphoid tissue; the outer coat was of smooth muscle and fibrous tissue, with scattered lymphocytes and some elastic fibres; there was no evidence of lymphangioma.

The character of the fluid contents excluded parasitic, chylous, or blood cysts; there were no cells not normally found in the omentum; the diagnosis was therefore a simple lymphatic or serous cyst.

Rokitansky attributed such cysts to degeneration of lymphatic glands, but if that were so, why should they not be found elsewhere, and why almost exclusively in early childhood?

Langhans looked upon them as due to lymphatic stasis and retention, but whether as a result of endo- or extra-vasal obstruction, whether due to trauma or inflammation there was no evidence to show; and Brunetti's experiments negatived the idea of encapsulated escaped lymph. Richet suggested an origin from haematomata and this may be an exceptional mode of production, though histological evidence is against it.

Cuneo looks upon them as a result of defects in peritoneal development, having observed pockets in the peritoneum of newly-born infants; the explanation is good for mesenteric cysts, but hardly for those of the omentum, unless, as Montanari suggests, by inclusion of peritoneal processes. The theory of Quénu and of Moynihan and Dowd, that all cysts except parasitic ones and the pseudocysts in neoplasms are derived from tissue-rests or embryonic organs, particularly Wolffian and Mullerian, would explain those with cubical, cylindrical, or goblet cells, with adenoma-like columns or tubes or papillae of cells, or with tissue resembling the adrenal cortex, but hardly those in which, as is the case with true simple serous cysts, all such elements are absent. Finally, Kermisson thinks of them as analogous to hygroma colli and due to a congenital ectasia of the lymphatics, whilst Delbet and others regard them as true lymphangiomata. Ranvier indeed did record a stage of regression in the development of primitive lymphatics which resulted in the formation of many blind-ended vessels and ampullae distended with lymph; but if that be so in the cat, Brunetti was quite unable to demonstrate anything of the kind in the human foetus. The author would trace them back to a vice in the assembly of the elements in the primitive omentum which go to the construction of the primitive lymphatic glands, and is thus able to account for the presence of all the cells found in the walls of the cysts he is describing.

There is a lengthy discussion of differential diagnosis; the outstanding point is the age, infancy; 70 per cent. are in females. E. R. C.

Nielsen, N. A. About the choice between medical and surgical treatment of ulcus ventriculi s. duodeni. *Acta Chir. Scand.*, 1922, **55**, 105.

Nielsen points out that the three chief inducements for preferring operative to medical treatment for ulceration of the stomach and duodenum are the prospects of malignant degeneration, fatal haemorrhage, and perforation. In an earlier work he has dismissed the first as a bogey. With regard to the risk of free perforation, he notes that the clinical and pathological statistical information hitherto available is unreliable. Though it is generally agreed that free perforation is an indication for operation, opinions vary greatly as to the chances of free perforation, and the importance the surgeon should attach to these chances when operative treatment is under discussion. Nielsen has investigated the after-histories of 182 patients, treated medically in hospital for gastric or duodenal ulcer 2½ to 19 years earlier. He found that 42 had subsequently been operated on, but in no case was free perforation the reason for operation. Among the remaining 140 patients there were 16 who had died, but in no case was death due to free perforation. Considering how common this accident is, these findings are surprising. The explanation is probably to be found in the fact that most cases of perforation occur in patients whose ulcers have lasted only a short time and have given rise to uncertain symptoms, whereas a clinically well-defined case of ulceration, which has lasted some time, shows but a slight tendency to perforation. Nielsen has collected the records of 62 cases of free perforation, and has found that in 31 premonitory symptoms had lasted less than a year, and in about two-thirds less than 2 years. Hence his conclusion that the danger of free perforation is very small in the case of clinically certain chronic ulceration; it does not warrant prophylactic operative treatment.

He comes to the same conclusion with regard to operative treatment as a prophylactic for fatal haemorrhage. Among 55 deaths from fatal haemorrhage there were as many as 27 in which the source of the haemorrhage was a recent ulcer or erosion of the mucous membrane. In 7 cases the post-mortem records were inadequate, and only in 21 cases did the fatal haemorrhage come from a chronic ulcer. As many as 20 of the 27 patients dying of haemorrhage from a recent ulcer or erosion were over the age of 40. It is a striking fact that while only about a quarter of all the ulcers of the stomach and duodenum develop after the fortieth year, it is after this year that three-quarters of all the fatal haemorrhages from recent ulcers occur. Of the 182 patients observed 2½ to 19 years after their discharge from hospital, where they had been given medical treatment for gastric or duodenal ulcer, only 2 were found to have died of severe haemorrhage. Accordingly, it is hardly justifiable for the surgeon to operate on cases of ulcer of the stomach and duodenum solely with the object of averting a fatal haemorrhage. C. L.

Moppert, Gustave G. La perforation de l'estomac par gangrène, complication de la hernie diaphragmatique. [**Gangrenous perforation of the stomach complicating diaphragmatic hernia.**] *J. de Chir.*, 1922, **20**, 453–63.

Three cases of this rare condition are reported, all of which came under Moppert's own observation during a period of four years. Following in one case a violent physical effort, in another a large meal improperly masticated, the patients were seized with acute pain in the epigastrium and exhibited the symptoms which arise from incarceration of a viscus, the picture changing later to that of peritonitis. At operation, in two of the cases the stomach had become disengaged from the hernial orifice and the cause of the gangrene might easily have been overlooked. Evidently when perforation occurred the escape of gas from the stomach allowed it to collapse and fall down into the abdominal cavity, at the same time allowing the gastric contents to enter and infect the peritoneum, which had until now escaped. All were fatal. The author points out how readily such a case might be regarded as one of perforated gastric ulcer or of phlegmonous gastritis. C. C. E.

NEUROLOGY

Kraus, W. M., and **Rabiner, A. M.** **On the production of neuro-muscular patterns by the release of spinal integrations after decerebration.** *J. Neurol. & Psychopathol.*, 1922, **3**, 209.

The profound obscurity of the title will warn the reader that this paper is not likely to achieve its expressed purpose of simplifying the analysis of disorders of muscular activity produced by lesions of the central nervous system. In it he will find a systematic use of physiological terms in senses quite remote from those generally understood, and phrases such as 'a kinetic form of decerebrate posture', or 'tone flows into moulds of pattern', which, when they are at all intelligible, indicate a profound misconception in the minds of their authors as to the physiological considerations so freely invoked. As far as we have been able to grasp the thesis maintained by Kraus and Rabiner it is as follows: morphologically, the skeletal musculature may be divided into ventral and dorsal muscle groups. Tables are given from Cunningham's *Anatomy* showing into which of these each of the limb muscles falls. Starting from this anatomical basis, an attempt is made to show that in either flexion or extension phases of the step, and in the tonic extension of the hind limbs in decerebrate rigidity, one or other of these two groups is in action alone and as a whole in a given segment of the limb. Further, taking the limb as tri-segmental, the formula is an alternating one. Thus in the case of limb flexion the formula is for hip, knee, and ankle, dorsal-ventral-dorsal, and in extension the converse, namely, ventral-dorsal-ventral. Taken as a whole, it is suggested that dorsal muscles have an extensor function and ventral muscles one of flexion. This alternating pattern for the limb is expressed as *DVD* for flexion and *VDV* for extension.

An effort is then made to apply the formula to the analysis of certain clinically observed disorders of tone and movement. For this purpose the authors describe three cases of epidemic encephalitis with widespread involuntary movements of irregular form, one of diffuse myelitis, and one of compression paraplegia. In every instance they are satisfied that their movement-formula obtains.

Succeeding chapters, which are rendered completely obscure by the vague and perverse employment of scientific nomenclature, deal with what are described as 'the relation of posture patterns to tone' and 'kinetic and static types'.

In respect of their main points, the alternating formula and the physiological unity of dorsal and ventral muscle groups, the authors have failed to realize that the anatomical and physiological data they quote contain a complete refutation of their views. Even in a simple reflex act produced under artificial experimental conditions, the muscles are not activated in dorsal and ventral groups as such. In Sherrington's diagram of the hind limb of a quadruped, which they reproduce, it can be seen that in a single limb segment muscles of both groups are in action in each phase of the step, while a single group may contain mutually antagonistic muscles. Thus, on the front of the thigh we have the vasti which extend the knee, and also rectus femoris which acts not as a knee extensor but as a hip flexor. Similarly, on the posterior aspect of the thigh is the anatomical muscle known as biceps femoris which includes two physiologically antagonistic muscles, one flexing the knee and the other extending the hip.

In the infinitely more complex and widespread voluntary movement, what Sherrington has called 'double reciprocal innervation' obtains and all the limb muscles may be, and generally are, in action simultaneously. This is clearly the case in such generalized involuntary movements as are described in the authors' patients. In a word, Kraus and Rabiner's morphological formula provides no basis for the physiological analysis of co-ordination.

However, we do not merely disagree with their conclusions, but also, and more emphatically, with the fashion in which Kraus and Rabiner have attempted to justify them. Thus, we notice that by what may be called a forensic mode of quotation and interpretation, certain physiological papers are made to convey meanings the exact opposite of those intended by their writers. For example, we are told that Sherrington's observations prove that the reflex arc of postural tone is, after all, purely spinal, and that the pontine centres known to be essential parts of this arc serve some undefined function of 'integration'. Similar examples of distortion might be quoted.

Finally, we cannot understand what has led Kraus and Rabiner to suppose that the conditions they describe in their case reports bear the remotest relation to decerebrate rigidity. We have not found anything to suggest this diagnosis, and we can only conclude that, like most of the other terms they employ, this very precise one has come to have some new and nebulous significance more readily adaptable to the ends of speculation.

In a previous review in *Medical Science*, 1921, **4**, 55, we deprecated the increasingly loose use of the term 'decerebrate rigidity' by clinicians, as bound to lead to great confusion. This paper, and that of Wechsler and Brock noticed below, may be regarded as the inevitable first-fruits of this habit, and in confusion of thought and expression they far transcend our gloomiest forebodings. F. M. R. W.

WECHSLER, I. S., and **BROCK, S.** **Dystonia musculorum deformans, with especial reference to a myostatic form and the occurrence of decerebrate rigidity phenomena.** *Arch. Neurol. & Psych.*, 1922, **8**, 538.

The authors describe six new cases of dystonia musculorum deformans (cf. *Medical Science*, 1920, **2**, 67) occurring in Russian Jews, which they believe to differ from previously reported cases in the predominance of a basis of muscular rigidity upon which the peculiar form of mobile spasm of the disease is superadded. The rigidity was confined to a single limb or limb segment in some instances, a fact which Wechsler and Brock express by the bizarre statement that the cases 'show the occurrence of large and small fragments of decerebrate rigidity'. Careful scrutiny of the clinical details and the accompanying photographs reveals nothing at all resembling decerebrate rigidity in any of the cases. Like Kraus and Rabiner, the authors assume that any localized or generalized extensor spasm must necessarily be identical with the decerebrate rigidity of animals, an assumption which indicates how meaningless the term has already become in clinical literature.

A generalized extension attitude is produced by the muscular spasm of strychnine poisoning, yet not even the most liberal interpreter of the term 'decerebrate rigidity' would maintain that the two conditions had a single factor in common. The same may be said of certain forms of hysterical 'fit'. In short, diagnosis by posture is wholly misleading and inadequate. It is to be regretted that those who rightly turn to the fruits of experimental physiology for inspiration do not more carefully study original sources of information, or, better still, make a direct examination of the decerebrate animal, when this is possible. F. M. R. W.

WEIZSÄCKER, V. v. Muskelkoordination und Tonusfrage. [**Muscular coordination and the problem of tone.**] *Deutsche Ztschr. f. Nervenheilk.*, 1922, **74**, 263.

The author, who combines a critical faculty with a sound knowledge of the string galvanometer, reviews the present state of this subject in a paper read before the eleventh annual meeting of German neurologists, held last year (1921). He believes there are many reasons for not accepting the view that there are two kinds of contractile substance and two modes of contraction in striated muscle. This view supposes that one substance, probably sarcoplasmatic, is responsible for tonic contraction, which is achieved without energy expenditure, fatigue, or action current. A second, probably the sarcostyle element, subserves active shortening contraction. Its mode of innervation is tetanic, the contraction is accompanied by expenditure of energy, by an oscillating action current, and is subject to fatigue. Starting from such an assumption it might be expected that such static motor activities as standing and the maintenance of postures against resistance are functions of this tonic apparatus, while all phasic motor activities which are accompanied by fatigue are a function of the tetanically innervated sarcostyles. Weizsäcker points out that such 'static' motor activities as those mentioned above are accompanied by increased metabolism, fatigue, and a tetanic action current in the muscles. Whence we see that this hypothetical 'tonus apparatus' is not in action when we should most expect to find it so. The finding of non-medullated nerve-fibres in muscles carries us no farther, for it is accepted that the division of these leaves tone unaffected. We are therefore left with two criteria of the existence of this hypothetical 'tonic apparatus', the absence of an action current and that of metabolic activity. In neither case do we obtain any proof of its existence. In the case of tonus in the eye muscles and the diaphragm, in decerebrate rigidity, and in veratrin contraction various observers have found an action current. In this respect a positive result is of more importance than a negative, of which the most that can be said is that an action current was not detected, not that it was not present. In his own investigations v. Weizsäcker has found an action current showing the same rhythm as occurs in voluntary muscular contractions, in tetany, the spasticity of hemiplegia, the rigidity of extra-pyramidal motor diseases such as paralysis agitans, in athetosis, katatonic rigidity, and during hypnosis. In the absence of any evidence of the existence of any other form of muscular contraction it cannot be urged that an underlying and distinct tonic contraction was 'overlaid' by a tetanic innervation of the muscles. Grafe, at the Heidelberg Clinic, investigated the metabolism of a series of patients with the conditions named above, and was unable to find any abnormality, from which it appears that the presence of an action current in the muscles is not necessarily an indication of increased metabolic activity, or an observation which we can utilize for the differentiation of tonic from phasic muscular contraction. Hence we must conclude that there is no evidence of the existence in the skeletal muscles of man of a form of muscular tissue comparable with the smooth tonus muscle (of invertebrates). v. Weizsäcker concludes that the view expressed by various writers in the literature of the subject, that so-called static motor activities can be correlated with the action of a special tonic mechanism in the muscle, and kinetic activities with a special fibrillary shortening apparatus, or, further, that the former activities are a function of the basal ganglia and the latter of the pyramidal system, are 'pure fantasies' which must be absolutely rejected. Neither in respect of muscle nor in that of nervous control can tonic and phasic activities be rigidly separated. They form an indivisible whole.

In the matter of the scope and limitations of the string galvanometer in the investigation of the various forms of muscular action, Weizsäcker may be taken to speak with authority, but it is not quite clear from some of his concluding remarks that he is altogether familiar with modern work on the physiology of muscle tone and co-ordination. He seems to go too far in attempting to reject all physiological distinction between the postural and phasic components in co-ordination. Nevertheless, this expression of his view is salutary, for, in the hands of some neurologists who have based their hypotheses upon anatomical and physiological observations which they have not fully understood, the attempt to elaborate anatomical and physiological distinctions between so-called 'static' and 'kinetic' muscular activity has been carried to absurd extremes. F. M. R. W.

Uyeno, K. On the supposed relation of the sympathetic to muscle tone. *J. Physiol.*, 1922, **56**, xliii.

Dusser de Barenne and others have shown that decerebrate rigidity is unaffected by depriving the muscles of their sympathetic supply. Whether stimulation of the sympathetic will increase the rigidity has not been investigated. Therefore Uyeno has tried the effect of stimulating the stellate ganglion and of applying nicotine to it. He finds that neither stimulation of this ganglion nor its paralysis by nicotine has any appreciable effect upon decerebrate rigidity. F. M. R. W.

Paton, L. Tabes and optic atrophy. [**B.**] *Brit. J. Ophthalmol.*, 1922, **6**, 289.

On looking over series of visual fields obtained from tabetic patients, the author has been struck by the remarkable variability they show and the marked disproportion existing in different cases between the loss of visual acuity and the loss of visual field. To elucidate whether variations in the pathological process explain this clinical variability, he is led to review existing knowledge on the pathology of tabes. Paton gives a valuable and concise summary of old and recent work on the pathology of this disease, including the observations and conclusions of Richter (cf. *Medical Science*, 1921, **4**, 547), who believes that the essential pathological process is the development of a special form of granulation tissue, composed of fibroblasts, around the radicular nerve of Nageotte. This gives rise to secondary degeneration of the nerve-fibres. Paton concludes that the old hypothesis of a meta-luetic toxin, the product of previous tissue degeneration of syphilitic origin, must be abandoned. It must now be allowed that all the manifestations of syphilis depend upon the local production of toxins in the presence of the spirochaete. The tissue reaction may vary according to the virulence of the spirochaetes, the resistance of the tissue concerned, and the time factor. However, it still remains uncertain whether the action is primarily on nervous elements or upon vascular and meningeal structures, or upon both. The author believes that the last possibility is the one which would best explain the clinical variations in visual acuity and fields, with which he is concerned.

The variability in functional disturbance in tabetic optic atrophy shows itself in the relationship that exists between visual acuity, visual fields, and ophthalmoscopic appearances, as well as in the progress of the disease. Another functional disturbance, and perhaps the earliest to develop, is a defect in dark adaptation. Behr divides the clinical course of optic atrophy in tabes into four stages: (1) isolated disturbance of adaptation, with normal appearance of the disk, normal visual acuity, colour sense and fields; (2) signs of atrophy are added, but no fresh functional disturbance; (3) optic atrophy, loss of visual fields for white and colours, and diminution of visual acuity; (4) optic atrophy and amaurosis.

Paton gives the visual fields and clinical details of eight selected cases of tabetic optic atrophy. These show the following variations: diffuse loss of function throughout the whole field for white and for colours, sharply defined peripheral constriction of the fields with good central vision, gross dissimilarity between the conditions obtaining in the two eyes, bitemporal quadrantic hemianopia. He also reproduces from the literature examples of central scotoma and of horizontal hemianopic loss.

In conclusion, Paton observes that the probable explanation of the clinical variations is that they truly represent variations in the disease process at work; that in tabetic optic atrophy we have a process in which both parenchymatous and interstitial tissues are attacked by the toxin. In some cases the parenchyma suffers more severely and at an earlier stage, and then there is presented the rapid diffuse loss of function involving the central acuity, the functional adaptation, and the colour fields, but often leaving an almost full field to large test objects. In other cases, and probably more frequently, the interstitial tissue lesion predominates, and the clinical result is the circumscribed loss of field with actively functioning and intact parenchyma away from the neighbourhood of the chronic interstitial inflammation. In other words, there seems to be evidence that the toxin attacks both parenchyma and interstitial tissue simultaneously. An extensive bibliography adds to the value of this informative paper. F. M. R. W.

Armstrong, C. N. Three cases of supra-pituitary tumour presenting Fröhlich's syndrome. *Brain*, 1922, **45**, 113.

The author describes three cases of Fröhlich's syndrome associated with basal tumours, none of which started in or infiltrated the pituitary body.

(i) A boy of 10 came under observation with headache, vomiting, and failing vision of four months' duration. In addition, he was noticed to become fatter, and 12 days before admission to hospital he began to grow drowsy. On examination, the boy was found to be small, but well nourished. His height was 3 ft. 10 in. and weight 3 st. The skin was dry, smooth, and delicate in texture. The distribution of fat was feminine. The hands were small and the fingers tapering. The external genitalia were normal. He was drowsy and spoke with a hoarse voice. Smell was of normal acuity. Vision was much reduced in acuity, and, as far as could be determined, the temporal fields seemed most at fault. There was papilloedema subsiding into atrophy in both eyes. The pupils were dilated and reacted feebly. Cranial nerves, motor and sensory systems were free from abnormality. Following an abortive attempt at operative removal the boy died. At autopsy a large tumour was found lying above and depressing the chiasma. It lay in the mid-line and was of the 'size of a walnut'. It was attached to the floor of the third ventricle and to the base of the infundibulum, from the upper part of which it appeared to arise. It was encapsuled, except at its point of origin from the infundibulum, and cystic. Although flattened, the pituitary body appeared normal. The sella was enlarged. Microscopic examination indicated that the growth arose in the ependymal lining of the infundibular recess.

(ii) A woman of 35 came under observation on account of amennorrhoea of 15 months' duration, adiposity, headache, and failing vision. During this time she had increased from 11 st. to over 16 st. in weight. The skin was dry and fine in texture, and the hair growth and distribution normal. Visual acuity was greatly reduced, but the optic disks were normal in appearance. The pupil reactions were normal. The right external rectus was paralysed. There were no other abnormalities. Autopsy revealed a tumour of the same size and situation as in the first case. Its attachment was also similar, and it was cystic in character. The sella was greatly enlarged. It consisted of masses of epithelial cells enclosing cavities and calcareous deposits.

(iii) A fat girl of 18 years and of juvenile appearance. The skin was dry and scaly and, except for the scalp, almost hairless. As in the other cases, smell was normal in acuity, but vision almost lost. There was bilateral primary optic atrophy. The pupils were dilated and inactive. Both external and internal recti were weak. No other abnormal physical signs noted. The tumour was exposed from in front, and yellow fluid rich in cholesterin crystals removed. The patient became maniacal and died twelve days later. A tumour of the size and anatomical relations described in the two preceding cases was found at autopsy. It was cystic, and contained crystals of cholesterin, a brownish fluid, and calcareous matter.

The author gives an historical *résumé* of similar recorded cases. He finds that growths of an epithelial character are most common in this situation. In origin they are cranio-pharyngeal. Their symptomatology is fairly constant; signs of compression of chiasma and optic tracts, with hydrocephalus and signs of increased intracranial tension as terminal manifestations. The general symptoms are those of Fröhlich's syndrome, varying according to whether the condition has developed before or after puberty. In the latter circumstances, there is a reversion to adolescent type, amennorrhoea, diminution of body hair, and sterility or impotence. Polyuria (diabetes insipidus) may also be present. Of the three cases here recorded polyuria was present in one.

The author inclines to the view that dystrophia adiposo-genitalis in cases of supra-pituitary tumour is associated with injury to, or destruction of, the pituitary gland. Possibly the discharge of the secretion of the pars posterior into the third ventricle may be prevented by the growth when this involves the infundibulum. F. M. R. W.

Rossi, G. Effetti delle ablazioni corticali cerebellari eseguite dopo la interruzione del circolo sanguigno. [**On the removal of portions of cortex cerebelli after interruption of circulation.**] *Arch. fisiol.*, 1922, **20**, 191.

The asymmetrical position of the limbs consequent upon unilateral removal of portions of cortex cerebelli persists after the death of the experimental animal and becomes plainer after the onset of cadaveric rigidity. The same postural asymmetry is observed if the operation is performed after complete interruption of the greater circulation, and does not differ qualitatively from that obtained after removal of the same parts of cortex cerebelli in the living animal. This fact proves the existence of cerebellar cortical centres, the lesion of which gives rise to manifestations entirely independent of any primary or circulatory alteration of the cerebellar nuclei. C. D. F.

Da Fano, C. (1). **Simple process for rendering permanent Golgi-Cox preparations.** *J. Physiol.*, 1921, **54**, cxiii.

Da Fano, C. (2). **Permanent Golgi-Cox specimens.** Ibid., 1922, **56**, xii.

Pieces, which by a trial section have been found well impregnated, are washed for some hours in distilled water and then brought, through many changes of alcohol of ascending strength, into absolute alcohol and embedded in celloidin in the usual way. The celloidin blocks are hardened in 70 per cent. alcohol, where they can be safely left for many days or weeks. Sections of the desired thickness are collected in 60 per cent. alcohol, transferred to distilled water, and thoroughly washed. They are then treated for 5–10 minutes with 5 per cent. ammonia, washed over again, and toned by means of a slightly acidified 0·2 per cent. gold chloride solution, in which sections are left for 10–15–20 minutes according to thickness. After a quick washing they are passed for 5 minutes into 5 per cent. sodium hyposulphite and washed once more. At this point sections were originally passed through alcohols of ascending strength, to each of which one drop of saturated iodine tincture to every 5 c.cm. of alcohol had been added. The author has now abandoned this last treatment and adopted instead bleaching the toned and fixed sections with weak solutions of potassium permanganate and sulphurous acid as in Pal's modification of Weigert's myelin stain. The toned and bleached sections may be counterstained with diluted alum carmine or similar stain, and then dehydrated and mounted in balsam under a cover-slip as ordinary celloidin sections. The specimens last unchanged for years. C. D. F.

Lafora, G. R., e **Prados, M.** Investigaciones experimentales sobre la función del cuerpo calloso. [**Experimental investigations on the function of corpus callosum.**] *Arch. de neurobiol.*, 1921, **2**, 363.

In monkeys and cats lesions of the corpus callosum cause paretic and apraxic phenomena of the side opposite to the hemisphere nearest to the lesion. These symptoms disappear 15–20 days after the operation, and reappear if this is performed once more on the same animal. They do not depend, as supposed by Koranyi, upon an increased amount of fluid within the lateral ventricles, because the same symptoms are observed when such an increase does not exist, and they may sometimes be absent when the amount of fluid is actually increased. The severity of the symptoms is connected, up to a point, with the extent of the lesion. If this is limited to the genu of the corpus callosum the apraxia affects the anterior limb; if it corresponds to the middle of the callosum, the anterior and posterior limbs become apraxic; if the lesion is in the posterior half, only the hind limb is affected. Lesions of the splenium cause very slight symptoms. Hemiparetic and apraxic symptoms are observed at the same time after the total section of the callosum. The crossed apraxia is probably due to an inhibitory action manifesting itself under the influence of the lesion upon the nearest cerebral hemisphere. C. D. F.

Bagley, C., jun. Cortical motor mechanism of the sheep brain. *Arch. Neurol. & Psych.*, 1922, **7**, 417.

Anatomical and experimental investigations, the conclusions of which may be summarized as follows: the coronal sulcus is one of the first fissures to appear in the development of the neopallium in the sheep embryo. The cell-layers of the cortex mesial and lateral to the coronal sulcus are well defined at a stage of development when the sulcus has the characteristics of the adult sheep brain. At this stage the layer of the large pyramids extends throughout the superior frontal convolution and through the mesial portion, but does not reach the crest of the middle frontal convolution. The histological findings in the superior frontal convolution are the same as those described by King; the cortex of the middle frontal convolution and that surrounding the outer extremity of the cruciate sulcus also present a similar appearance. Stimulation of the posterior portion of the superior frontal gyrus produces contractions of the extremities; stimulation of the cortex of the gyrus immediately in front of this area causes movements of the head and eyes to the opposite side. Stimulation of the most anterior portion of the superior frontal gyrus gives no reaction. Stimulation of the small gyrus (' Area 4 ') lying between the frontal end of the presylvian fissure and the outer anterior spur of the coronal sulcus causes contraction of the face muscle of the opposite side, more particularly of the lower lip. Stimulation of the middle frontal gyrus over an area about 1 cm. square, usually opposite the middle portion of the coronal sulcus, causes contraction of the muscles of the face of the same side. This centre is easily excited. Stimulation of the gyrus surrounding the outer extremity of the cruciate sulcus and of the areas posterior to the same sulcus produces no reaction. As previously found by other authors, extirpation of the excitable areas of the cortex does not cause a disturbance of locomotion. The findings of other investigators regarding the course of the main mass of the pyramidal tract and its decussation in the hind-brain are confirmed. In addition to the degeneration of the main mass of the pyramidal tract there is, in the tegmentum, evidence of degeneration of a bundle of fibres. This degeneration, ipsolateral in its entire course, is first noticed in frontal sections at the level of the red nucleus, from where it continues, dorsalward from the pyramidal tract, till the dorsolateral angle of the tegmentum, ending at the level of the facial nucleus, beyond which point it cannot be demonstrated.

C. D. F.

CARLSON, A. J. Studies on the visceral sensory nervous system. XIII. The innervation of the cardia and the lower end of the oesophagus in mammals. *Am. J. Physiol.*, 1922, **61**, 14.

This and previous investigations on the visceral nervous system have led the author to question the adequacy and utility of the prevailing view as to the structure and function of the autonomic system. At present the visceral efferents in the vagi, splanchnics, &c., with their peripheral ganglionic connexions, are considered as analogous to the motor afferents of the skeletal muscles. The conception of axon reflexes has been introduced, but the existence of true reflexes in the visceral system apart from central connexions is denied. The apparently fixed reactions of the heart to vagal and sympathetic stimulation has led to the assumption of a similar relation for the rest of the viscera and to look upon the relation of the visceral efferents to the end organs as being as simple as the relation of the pyramidal tract to the skeletal motor neurones. The author questions whether this conception is applicable in every case, and suggests as a working hypothesis that '*the visceral nerves are complex association paths connecting cerebrospinal and visceral reflex centres, rather than relatively simple nerves like the skeletal efferents*'.

The stomach and small intestines are under motor and inhibitory control both of the vagi and the splanchnics. This effect is similar, not to the effects of sciatic stimulation in the leg musculature, but to the influence of cerebellar efferents on the skeletal motor system. In both cases motor or inhibitory effects are produced according to the tonus state of the peripheral mechanism.

The view of a physiological antagonism of the vagi and sympathetic becomes therefore untenable, at least for the gut, and a rectification of the terms ' vagotonia ' and ' sympatheticotonia ' is called for. W. C.

PATHOLOGY

Pace, D. Nuove ricerche e considerazioni sul nodo del seno del cuore dei mammiferi. [**New investigations and considerations on the sino-auricular node of the heart of mammalia.**] *Riforma med.*, 1922, **38**, 385.

The demonstration of the sino-auricular node of Keith and Flack by means of injections of Indian ink is not possible. For experimental purposes the situation of the node is sufficiently well indicated by the *sulcus terminalis.* As far as one can judge from the examination of serial sections, the node ends before the stria cavo-atrialis and without showing any connexion with the node of Tawara. The statements of Schrumpf as to the existence of a left sino-auricular node, and of Bachmann as to the existence of an interatrial bundle, are not sufficiently well proved.

C. D. F.

Savolin, M. Om Biedl's experimentella glykosuri och dess förhållande till diabetes mellitus. [**Concerning Biedl's experimental glycosuria and its relation to diabetes mellitus.**] *Finska Läk-sällsk. Handl.*, 1922, **64**, 456-82.

Savolin, of Helsingfors, has carried out certain investigations which were prompted by the work of Biedl and Hédon. The former showed, in 1898, that when the thoracic duct of dogs was ligatured or the chyle in this duct was diverted, permanent glycosuria was provoked. Hédon, in 1911, found that when blood from a pancreatic vein of a normal animal was introduced into the portal vein of a dog with pancreatic diabetes, its excretion of sugar dwindled or ceased completely. But when blood from a pancreatic vein was introduced into any other veins than the portal vein or its branches, no such result followed. This experiment suggested that the blood in the pancreatic veins contains an active substance which, in conjunction with the liver, greatly reduces the glycosuria of pancreatic diabetes. Savolin has worked with cats in which experimental pancreatic diabetes was induced. Small quantities of the contents of the thoracic duct of healthy animals were given by the mouth, by subcutaneous and by intravenous injection to the diabetic cats, but no effect was produced on their glycosuria. These findings, which are confirmatory of Falta's, suggest that the internal secretion of the pancreas does not reach the blood-stream by way of the thoracic duct. Another line of research followed by Savolin has been to study the records of cases of compression of, or injury to, the thoracic duct in man. These records show that, as a rule, obstruction of the thoracic duct or diversion of its contents from their normal course is not followed by glycosuria. In most of these cases, however, the thoracic duct may have had collateral channels through which an adequate supply of chyle may have reached the blood. Savolin confesses that the mechanism of Biedl's glycosuria is still obscure. C. L.

Gargano, C. Abolizione della birifrangenza delle fibre muscolari nelle appendiciti croniche. [**Disappearance of anisotropy of muscle-fibres in chronic appendicitis.**] *Riforma med.*, 1922, **38**, 817.

In normal conditions the muscle-fibres of the muscular coats of vermiform appendix are doubly refracting when examined with polarized light between crossed nicols. This property is in part lost in cases of acute appendicitis and entirely lost in chronic forms, even when other lesions are no longer detected by ordinary methods of histo-pathological examination.
C. D. F.

Nuzzi, O. Il celluloide nella microtecnica. [**Celluloid for microscopic work.**] *Riforma med.*, 1922, **38**, 818.

Thin sheets of celluloid can be easily cut with scissors and the pieces used as cover-slips. The thickness of the thinnest sheets obtainable from the trade averages 0·11 mm., which is something less than that of glass cover-slips (0·14–0·17 mm.). In addition the index of refraction of celluloid (1·5002) is very near to that of cedar-wood oil (1·5100); it can therefore be employed with advantage for mounting specimens which are to be observed under oil immersion lenses. The non-success of Neumayer in a similar attempt at making cover-slips from sheets of celluloid is explained by Nuzzi pointing out that Neumayer used too thick sheets (0·2–0·4 mm.). C. D. F.

Torraca, L. L'azione necrotizzante delle matite copiative e di alcuni colori di anilina. [**The necrotizing action of copying pencils and of some aniline dyes.**] *Arch. per le sc. med.*, 1922, **44**, 283.

Wounds from copying pencils seem rather frequent since Erdheim, (vide *Medical Science*, 1920–21, **3**, 239) observed 23 cases in Austria, and showed that fragments of such pencils, when left for some time within tissues, cause extensive necrotic and inflammatory processes which may last for many weeks. Torraca has now investigated this phenomenon experimentally by introducing sterilized fragments of copying and ordinary pencils as well as certain histological dyes within the muscular tissue of guinea-pigs. The results obtained were: fragments of ordinary pencils act as indifferent foreign bodies. Fragments of copying pencils have a rapid and intense phlogistic action accompanied by an extensive necrotic process. This is due to the methyl-violet generally contained in copying pencils. Cresyl-violet, crystal-violet, and gentian-violet have a similar action. In guinea-pigs the local phenomena are frequently associated with a general toxic action which may be fatal. In the poisoned animals important degenerations of the liver and kidneys are found, together with a diffuse congestion and some small haemorrhages of the lungs. C. D. F.

Ciaccio, C. Sul meccanismo di produzione della leucocitosi digestiva. Nota I. [**On the mechanism of production of digestive leucocytosis. Note I.**] *Haematologica*, 1922, **3**, 1.

A leucocytosis was observed after the introduction of a 4 per cent. solution of HCl into the stomach of fasting dogs. The fact was quite noticeable 30 minutes after the beginning of the experiment and reached a maximum after 60 minutes, when it began to diminish and finally disappeared between the second and fifth hour. This leucocytosis was in some experiments preceded by a leucopenia. These observations show that digestive leucocytosis, whether preceded or not by leucopenia, is not due to the digestion of proteins but to the HCl secreted by the stomach. C. D. F.

Gelera, M. Influenza della luce artificiale sulla costituzione morfologica del sangue. [**Influence of artificial light on the constitution of circulating blood.**] *Gazz. d. Osp.*, 1922, **43**, 396.

Experiments were made in man by means of a quartz lamp. The following results were obtained: the haemoglobin content, the number of red corpuscles, and the percentage of eosinophil and basophil cells were unaffected. The polymorphocytes and large mononuclear leucocytes showed a moderate numerical increase. The small lymphocytes were greatly increased in number and their increase was still remarkable 48 hours after the beginning of the experiment. The first exposure to artificial light is, in general, very effective; the following ones have a progressively diminishing influence. Remarkable individual differences were observed among various healthy subjects, but none between the latter and tuberculous patients. C. D. F.

Johnstone, E. M. Changes in the morphology and function of the bone-marrow after splenectomy. *Thesis, University of Minnesota*, 1921.

The interpretation of films or sections of bone-marrow has always been difficult owing to the lack of a definite standard of comparison. Johnstone has provided such a standard and it is at least valid for his particular purpose, namely, an investigation into the bone-marrow changes after splenectomy. The animals used were 20 dogs, 40 rabbits, and 2 goats. The essentials of the method were (1) removal of a portion of rib-marrow prior to splenectomy; (2) removal of further portions at various periods after splenectomy; (3) control by similar removals from non-splenectomized animals; (4) parallel observations on the blood; and (5) two series of experiments, one under ether and the other under cocaine, for operative procedures.

Marrow specimens were graded according to four cardinal features, namely, erythrogenesis, leukogenesis, vascularity, and density of marrow cells. In each group were four grades of activity, Grade I being that of least activity, Grade IV that of highest development. Thus in a particular case the marrow might show erythrogenesis 3, leukogenesis 2, vascularity 2, and density 3. The specimen would then be averaged as 2·5 and on this basis compared with other specimens. Although the method is arbitrary, it gives comparable results in the hands of the same investigator.

Johnstone's conclusions are that splenectomy is followed by a latent period of about four weeks, during which marrow activity is unaltered. At the end of this time erythrogenic activity increases and reaches a maximum at from eight to twelve weeks after splenectomy. This maximum persists for another twelve weeks. After this a normal condition is slowly resumed, but is not established for as long as twelve months after splenectomy. But this normal still shows a considerable increase over the normal for the same animal prior to splenectomy. He further concludes that erythrogenesis is increased at least four weeks before the increase is reflected in the blood count. These results and others are fully discussed in the light of experiments and observations by other workers. G. W.

Allport, C. The blood count. *Lancet*, 1922, ii, 756–8.

Allport calls attention to the undeniable inaccuracies of the present types of blood-counting apparatus, and in particular to the errors which arise from bending of the cover-slip. To obviate these he has used a cover-slip 3·8 mm. thick. In order to bring a sufficiently small field to focus through this thick cover-slip he uses a No. 18 compensating eyepiece and a two-thirds objective. He gives details of actual counts which speak well for the new method. G. W.

Leake, C. D. Leukocytic reactions to morphin. *J. Am. M. Ass.*, 1922, **78**, 1687–8.

Leake reports on the effect on the leucocyte count of morphia injections. He experimented on four rabbits, fifteen dogs, and four men. He gives two tables for the animals each averaging the different counts. The tables for the men are given in full. This method of presenting results is not by any means satisfactory, for the variations are small. He concludes that morphia produces a slight leucocytosis. G. W.

De Wesselow, O. L. V. The calcium and inorganic phosphorus content of the maternal blood during pregnancy and lactation. *Lancet*, 1922, ii, 227–8.

De Wesselow finds that the most striking variation from the normal in the blood chemistry of the lactating female is an increase of inorganic phosphorus. He also makes the most interesting suggestion that estimation of the total solids strongly suggests that the blood is progressively diluted during pregnancy. This affords an interesting parallel with the condition obtaining during the establishment of puberty and may also help to explain the relatively little effect of blood loss during parturition. G. W.

McLester, J. S. The diagnostic value of blood fibrin determinations. *J. Am. M. Ass.*, 1922, **79**, 17–19.

McLester, using the method of Foster and Whipple, investigated the amount of fibrin in the blood of 100 sick persons and fifteen normal controls. The latter gave figures which suggest that the normal lies between 250 and 400 mgm. per 100 c.cm. of plasma. The details given do not permit an opinion as to whether such figures are exact, but they would appear to have comparative value. The conclusions which McLester reaches are that normal persons always present fairly constant values, that inflammation always causes considerable increase, that stimulation of the liver has a lesser influence in the same direction, and that in conditions of great anaemia or debility the fibrin value is usually low, particularly if the liver is seriously damaged. G. W.

MINOT, C. B. Megacaryocytes in the peripheral circulation. *J. Exper. M.*, 1922, **36**, 1–7.

Minot remarks on the fact that the presence of megacaryocytes in the peripheral circulation has received no notice in English or American literature and but little on the Continent. He has found them commonly in leukaemia and occasionally in other conditions, and considers them indicative of a marrow under intense strain. The abstractor is able to confirm such findings. G. W.

FINEMAN, S. A study of microlymphoidocytic leukaemia. *Arch. Int. Med.*, 1922, **29**, 168–220.

Fineman reports a case of micro-lymphoidocytic leukaemia with the avowed intention of supporting the unitarian theory of blood-cell formation, i. e. the theory that all blood-cells originate in one primitive type. The case was that of a girl of 17 suffering from an acute type of leukaemia which was not distinguished by any peculiar feature. The case history and investigations are very fully and adequately set out. A single lymph node was removed during life and immediately fixed in Heller's fluid. As no autopsy was allowed it is upon this node that Fineman's case rests. He describes in great detail the type of cell most prevalent in the blood-stream and concludes that this is undoubtedly the cell which dualists claim as a myeloblast and as the precursor of all cells of the granular series. He next reports in similar detail the histology of the removed lymph gland and shows (1) that 'myeloblasts' were present in the germ-centres of the gland, and (2) that, although the cell content of the gland was so great as to obscure the histology of many parts, there were present undoubted follicles which were proliferating and forming myeloblasts. It is well known that the dualists claim that in myeloid leukaemias the lymph follicles are quiescent or actually atrophied and that the increased cell content of glands is due to myeloid 'infiltration' of the pulp. Fineman states categorically that the follicles were active and that they were actually producing cells of the same type as those infiltrating the pulp of the glands. He concludes that the so-called myeloblast was in this case seen to originate from lymph tissues, and claims that this disposes of the whole basis of the dualist doctrine. The difficulties which have always surrounded the discussion of this subject are to some extent present in this case. For what is the evidence available with which the dualist is to be converted? First, there is Fineman's opinion. This is good evidence—to every one except the dualist, who will naturally find in it all manner of prejudice. Secondly, we have a low-power photograph of the gland sections. This certainly shows what appears to be an active follicle, but what the dualist is at liberty to describe as one in the quiescent phase. Thirdly, we have drawings by the author of the germ-centres found. The drawing of single cells provides a wide field for individual expression, a fact of which the dualist cannot be expected to refrain from making use. And, fourthly, we have an account of the staining reactions of the cells in these germ centres. But staining reactions in the shrunken cells of fixed tissues are apt to be anomalous, a fact which Fineman fully acknowledges. Even if they were not anomalous there remains the unfortunate fact that just how a myeloblast ought to stain in all circumstances rests in the last resort with the dualists, who alone acknowledge the specificity of this cell. While commending Fineman for a very carefully worked out contribution to the subject, we feel that the controversies of unitarian and dualist have extraordinarily little importance compared to the mass of literature devoted to them. G. W.

Price-Jones, C. The diameters of red cells in pernicious anaemia and in anaemia following haemorrhage. *J. Path. & Bacteriol.*, 1922, **25**, 487.

The work of the author on the diameter of the red blood corpuscles has already been referred to (*Medical Science,* 1921, **4**, 366; 1921–2, **5**, 153). In the present paper he deals with the diameters of red corpuscles in pernicious and post-haemorrhagic anaemias. Dried films were prepared and the diameters of 500 cells were measured to 0·25μ, the mean diameter of 500 cells being taken to represent the mean diameter of the red cells for any specimen of blood. The cells of 20 cases of pernicious anaemia and of 10 cases of post-haemorrhagic anaemia were examined. It was found that the mean diameter of the red cells in pernicious anaemia was larger and in post-haemorrhagic anaemia was smaller than in health. In both of these conditions the range in size and variability of the red cell diameters was greater than in health, a result due to the blood containing mixtures of different kinds of cells. W. B.

Ecker, E. E., Kline, B. S., and **De Caluwe, A. The relation of reduction of leucocytes and platelets to complementing power of serum.** *J. Infect. Dis.*, 1921, **31**, 368.

The rôle of the leucocytes in the production of complement has been a matter of considerable study and dispute. The greater bulk of the work done on the subject was at a time when no clear differentiation had been made between amboceptor and complement, and by various methods of making extracts of white blood corpuscles. Experiments *in vivo* have not received sufficient consideration. With this point in view the authors have attempted to reduce the number of the circulating leucocytes to ascertain whether or not a parallel reduction of complement could be demonstrated. Equal parts of benzene and olive oil were mixed and injected subcutaneously in doses of 1 c.cm. benzene per kilo of animal. Rabbits were selected because of their known susceptibility to benzene and because their serum contains a fair amount of complement. The site of injection was massaged to allow a wide area of absorption. In every instance the number of leucocytes was brought down to a figure less than 1,000 per c.mm. The same is not true for the platelets. Some animals had a slight increase in platelets, an observation already made by Duke. The control animals that received olive oil alone showed a transient leucocytosis. The complement titre of all the animals remained within normal limits, so that it is fair to conclude that the reduction of leucocytes and platelets in the circulating blood-stream does not go parallel with a change in the complement titre of the blood-serum of the treated animals. Since the bone-marrow and spleen exhibit serious deterioration as the result of the benzene treatment, it is apparent that these tissues are not concerned in any important way in the maintenance of the complement of the serum. Whether the derivation of leucocytes is only apparent, as suggested by Pappenheim, or whether they accumulate in the dilated capillaries of the liver and other organs, is, at present, difficult to state. The authors' observations indicate that they do not accumulate in the liver. The condition of the marrow strongly suggests there is an actual reduction in the number of circulating leucocytes, and most modern studies point toward an absolute reduction. Antibodies are reduced following benzene injection, as pointed out by Hektoen. On the contrary, the complementing power of the blood-serum is not altered as the result of subcutaneous injection of benzene. W. A. M. S.

Fracassi, G. Alcuni casi di edema da fame in ex-prigionieri italiani in Austria e Serbia. [**Some cases of starvation oedema in Italian prisoners of war in Austria and Serbia.**] *Ann. d'ig.*, 1922, **32**, 371.

In cases of starvation oedema, toxins appear to originate from the tissues at the expense of which the organism is living for a time. These toxins would in their turn cause various alterations of the internal organs but chiefly fatal lesions of the kidney and liver. C. D. F.

Luisi, A. Su di un nuovo metodo di colorazione del bacillo di Koch. [**New method for staining tubercle bacilli.**] *Ann. d'ig.*, 1922, **32**, 367.

Stain smears for 15 seconds in a saturated watery solution of crystal violet to which 3 or 4 drops of a 5 per cent. solution of carbolic acid have been previously added. The crystal violet should be warmed while using it. Differentiate for a second in a 40 per cent. solution of nitric acid in water. Counterstain for half a minute with a watery solution of orange G. The specimens are permanent. C. D. F.

Puxeddu, E. Il plasma nella velocità di sedimentazione degli eritrociti. [**Influence of plasma on the sedimentation velocity of red-blood corpuscles.**] *Riforma med.*, 1922, **38**, 819.

Sodium chloride and sodium citrate delay the sedimentation of red blood corpuscles. An optimum of sedimentation is obtained by the use of 1·20 per cent. solutions of sodium chloride and 3 per cent. solutions of sodium citrate. The addition of distilled water or of traces of bile to the normal blood-plasma also delay the precipitation of erythrocytes. These are agglutinated by the addition to the plasma of solutions of glucose or of blood-serum. Transudates act as saline solutions; exudates almost as plasma. The sedimentation of red blood corpuscles from malarial subjects is rapid in their own plasma, and rather slow in that from healthy individuals. The sedimentation of normal erythrocytes is, on the contrary, very rapid in plasma from malarial subjects. This shows that in the blood-plasma of subjects affected by malaria toxic substances are contained which alter its physico-chemical properties. C. D. F.

Durand, F. Un nuovo metodo di colorazione vitale del sangue. [**New method for the *intra-vitam* staining of blood-cells.**] *Riforma med.*, 1922, **38**, 893.

Mix equal parts of saturated and filtered solutions of brilliant cresyl blue and Sudan III; add 2 per cent. of alcohol. One drop of the solution is mixed with one of blood and some of the mixture used for observation.

C. D. F.

Ramoino, P. Contributo alla conoscenza delle cause del maidismo sperimentale. [**Contribution to the knowledge of the causes of experimental maidism.**] *Ann. d'ig.*, 1922, **32**, 201.

Adult and young guinea-pigs fed on maize flour with the addition of some cellulose, NaCl, $Ca_3(PO_4)_2$, and water all died within a period of 16–37 days with symptoms identical to those observed after feeding on maize flour only.

C. D. F.

Salvagnini, G., e **Peserico, E.** Il tempo di coagulazione del siero di sangue nelle ipertermie sperimentali. [**The time of coagulation of blood-serum in experimental hyperthermia.**] *Arch. per le sc. med.*, 1921–22, **44**, 275.

The blood-serum of animals exposed to fatal high temperatures coagulates sooner than that of normal animals. This increase in the velocity of coagulation of the serum is due to the presence of dissolved haemoglobin originating from the haemolysis consequent upon exposure to high temperatures.

C. D. F.

Conti, L. Ulteriore contributo allo studio di una particolare forma di emoglobinuria sperimentale. [**Further investigations on a particular form of experimental haemoglobinuria.**] *Arch. per le sc. med.*, 1922, **44**, 298.

Reference was made to the investigations of this author on the haemoglobinuria obtainable in animals by intraperitoneal injections of their laked and isotonized erythrocytes (*Medical Science*, 1921–2, **5**, 264). It was pointed out that the haemoglobinuria could be prevented by heating the erythrocytes for 3 hours at 56° C. The author has now found that this protective action is no longer observed when the spleen or liver of the experimental animals are roughly handled, for instance, by pulling them. The removal of the spleen or of part of the liver has a similar effect, the haemoglobinuria manifesting itself even sooner than after the injection of unwarmed erythrocytes in normal animals.

C. D. F.

Susanna, V. Ricerche sperimentali sulle ipodermoclisi e fleboclisi di zuccheri in animali sani e nefritici. [**Experimental investigations on hypodermoclysis and phleboclysis of sugars in healthy and nephritic animals.**] *Riforma med.*, 1922, **38**, 793.

Solutions of lactose and saccharose, when injected either subcutaneously or intravenously, are only in part eliminated. If the animals are healthy their toxic effect is moderate: but if the animals are affected by a nephritic process the injections are followed by death. This is due to both the direct toxic action of the sugars injected and to the secondary infections which constantly follow the subcutaneous or intravenous inoculation of sugars.

C. D. F.

Speciale, F. Studio sugli innesti nel fegato di frammenti di linfoglandole precedentemente fissate. [**On the grafting of fragments of fixed lymph glands in the liver.**] *Arch. per le sc. med.*, 1922, **44**, 304.

A strong wall of connective tissue is soon formed in the liver round grafted pieces of lymph glands previously fixed in alcohol or formalin. The proliferated connective tissue originates from that of the periportal spaces and does not penetrate into the grafted pieces. These behave as inert foreign bodies and their reticular tissue is slowly reabsorbed. C. D. F.

Strangeways, T. S. P. Observations on the changes seen in living cells during growth and division. *Proc. Roy. Soc.*, B., 1922, **94**, 137.

The author has described and figured the changes which take place in living cells during growth and division *in vitro.* The cells employed were derived from the choroids of 7- to 9-day chick embryos and cartilage cells from the knee-joints of adult fowls, the culture medium being chick plasma with the addition of embryo chick extract. Subcultures were made every second day. It was clearly made out that the cells and the structures within it were never at rest during growth and division. In vigorously growing cells the times occupied by various stages of mitoses were as follows:

1. From the beginning of the prophase to the achromatic spindle being seen the time varied from 3 to 20 minutes, the average being 7 minutes.
2. From the formation of the spindle to the division of the cytoplasm into two cells the time was 12 to 47 minutes, the average being 20 minutes.
3. The time for complete division of the cell, from the beginning of the prophase to the appearance of the daughter nucleus varied in 13 cells from 23 to 65 minutes, the average being 34 minutes. W. B.

Busacca, A. Sui fagociti della mielina in speciali condizioni di esperimento e sul comportamento delle sostanze fagocitate di fronte alle colorazioni dei grassi e simil-grassi. [**On the phagocytes of myelin in particular experimental conditions and on the behaviour of the phagocyted substances when tested with fat stains.**] *Riv. di patol. nerv.*, 1921, **25**, 349.

Reference was made to the investigations of this author (*Medical Science*, 1922, **7**, 63) on grafted pieces of fixed nerves and their reabsorption through the medium of phagocytes. He has now made some fresh experiments with the object of obtaining further information as to the nature and origin of these cells. The conclusion reached may be summarized as follows: Within grafted pieces of fixed nerves roundish or irregular cells occur which do not essentially differ from those found in degenerating stumps of cut nerves. Such cells are not due to a transformation of the grafted Schwann's cells, but belong to the great category of Maximow's polyblasts and originate either from the blood or from the tissues of the host. They are amoeboid and attack the degenerating myelin and axis-cylinders, fragments of which they phagocyte, thus assuming the aspect of fatty granular cells. The phagocyted materials undergo the same transformations as described in degenerating nerves, but in a very slow manner, so that substances stainable by Marchi's method are seen only 30 days after the operation, and substances stainable by Herxheimer's method after 40 days. C. D. F.

Spadolini, J. Avitaminosi e lesioni sperimentali dei nervi mesenterici. [**Deficiency diseases and experimental lesions of the superior mesenteric plexus.**] *Arch. di fisiol.*, 1922, **20**, 165.

After the removal of extensive portions of the superior mesenteric plexus, cats may survive from 2 or 3 days up to a month. After the operation they exhibit the following symptomatology: progressive diminution of the body temperature, dyspnoea, anorexia, sickness, diarrhoea, frequently associated with presence of blood in the excrement, albuminuria, and a general and rapid decay ending in death. In addition, paresis and a spastic condition of the hind limbs may be observed, these phenomena being accompanied by loss of hair and other cutaneous dystrophic changes. Most important are the lesions of the digestive organs and nervous system. In the small intestine an intense congestion and a diffuse necrosis of the mucous membrane are often observed; the pancreas is atrophic and the liver congested; the mesenteric lymph glands are oedematous and congested if the animals survive a few days, but sclerotic or atrophic in those surviving for longer periods. The lesions of the spleen are similar to those of the mesenteric lymph glands. In addition, parenchymal alterations of the kidneys are not rare, and interstitial haemorrhages in the lungs, heart, and muscles frequently occur. The adrenals are swollen, while the thyroid is noticeably atrophic. Chromatolysis and other acute changes are found in the coeliac and other sympathetic ganglia, as well as in the anterior and lateral cell groups of the spinal cord. According to the author these various symptoms and changes are analogous to those due to the absence of the B accessory food factor. He therefore puts forward the suggestion that certain forms of avitaminosis may be connected with a primary lesion of the autonomic nervous system. C. D. F.

Scaffidi, V. Ricerche sull' importanza del fegato nella sintesi dell' acido urico. Effetti della soppressione della funzione epatica sulla formazione dell' acido urico, delle basi puriniche e dell' urea. [**Investigations on the rôle of the liver in the synthesis of uric acid. Effects of the suppression of the hepatic function on the production of uric acid, purine bases, and urea.**] *Arch. d. sc. biol.*, 1922, **3**, 424.

The removal of the liver in fasting ducks causes a considerable diminution in the production of uric acid. Such a diminution is, however, never so remarkable as was stated by Minkowski. A similar effect, though in smaller proportions, is seen after ligature of the afferent blood-vessels to the liver. The diminution of the uric nitrogen is not connected with the suppressed hepatic function, but with the biological activity of the tissues. In fact, the diminution is greater in animals which die soon after the operation than in those which survive for a relatively long time. The suppression of hepatic circulation has no effect on the elimination of urea, and also this fact is against the supposed exclusive or prevailing rôle of the liver in the synthetic processes connected with the metabolism of nitrogen compounds.

C. D. F.

Da Fano, C. (1). **On Golgi's internal apparatus of the mammary gland.** *J. Physiol.*, 1922, **56**, xxii.

Da Fano, C. (2). **On Golgi's internal apparatus in different physiological conditions of the mammary gland.** *J. Physiol.*, 1922, **56**, 459.

Golgi's internal apparatus is a constant feature of the epithelium cells of the mammary gland in all stages of its physiological history. In the virginal condition the apparatus consists of one or more small reticular portions situated next to the nucleus on the side facing the glandular lumina. During pregnancy the apparatus greatly hypertrophies and shows a tendency to surround the nucleus with its network. This phenomenon seems to be brought about by the approaching hyperactivity of the cytoplasm. From the moment the young are born, and all through lactation, the apparatus is still hypertrophic, in part fragmented and shifted and stretched in various directions. The hypertrophy and partial fragmentation are very likely connected with the activity of the cells; the shifting and stretching appear chiefly due to the increased intracellular pressure. These facts are against the identification of the apparatus with a fixed system of intra-protoplasmic canaliculi. In the period of involution after lactation the epithelial cells undergo deep changes, during which the apparatus appears to become transformed into peculiar roundish, oval, or elongated shapes, delimited by a granular or filamentous argentophil material. Most of these cells are eliminated with their deformed apparatus. Some remain as the permanent epithelium of the gland at rest, and in these cells an apparatus is found similar to that of the virginal condition. It is suggested that the apparatus of the surviving cells is rebuilt from the fragmented and perhaps fluidified materials out of which the old one was formed. As far as the mammary gland is concerned, no fact was noted in favour of the supposition that part of the apparatus is thrown off from the cells together with other products of their secretory activity. But the continuous passage of detached epithelium cells with their apparatus into the glandular lumina and ducts is assumed to mean that in this way the apparatus takes an indirect part in the function of the gland. C. D. F.

Nageotte, J. Sur la genèse de la substance conjonctive et sur la 'greffe morte'. [**On the genesis of connective tissue and on 'dead grafts'.**] *Arch. per le sc. med.*, 1922, **44**, 223.

Reference was made to Busacca's and Poiettini's investigations (*Medical Science*, 1922, **7**, 63) on grafted pieces of fixed tendons and nerves and to the conclusion reached by them that Nageotte's theory of the 'revivification' of dead connective tissues does not hold good. In the present paper Nageotte answers their criticism and explains his views on the subject.

It is generally admitted that the intercellular substance of connective tissues is a product either of differentiation or of secretion of the cells and that this product or exoplasm acquires through a process of evolution a more or less complete independence from the cells from which it originates, though still depending upon them as regards its life. In spite of many facts against this supposition, Nageotte had also accepted it in the absence of a more satisfactory one. After investigating the evolution of the blood-clot in aseptic wounds he formed a different opinion. These investigations showed him that fibrin, though not living, may become transformed, *in vivo*, into 'a substance which does not differ in any way from the ordinary connective tissue substance'. This 'metamorphism' is due to various local conditions, among which the chemical activity of the ferments secreted by the fibroblasts migrated into the blood-clot has a capital part. That fibrin may transform into a substance similar to connective tissue had also been suggested by Baitsell, who failed to recognize certain details of the process, which were further investigated and explained by Nageotte. An almost identical metamorphism would normally give origin to the ordinary connective tissue substance. This is, at first, probably nothing else but a coagulated albuminous material, which may or may not be a modified exoplasm, but which in any case never had or has any life of its own. It only possesses the property of attracting from the surrounding tissues living cells, under the influence of which it becomes transformed into connective tissue, just as fibrin in certain experimental conditions.

The life of connective tissues may, therefore, be conceived as due to the interaction of the cells and the intercellular substance, though the former only can be said to be living. When a connective tissue structure is fixed the cells only are killed, not the intercellular substance which never was alive. When a fixed piece of tendon is, e. g., grafted under the skin of a rabbit's ear, the frame of the 'dead' graft acquires intimate connexions with the intercellular substance of the connective tissue of the host and is 'revivified' by cells, which take the place of the old ones killed by the fixative. The term 'revivification' of connective tissues does not mean 'que la substance conjonctive soit reviviscente, puisqu'elle n'a jamais vécu, à proprement parler ; il faut dire simplement que la vie s'est réinstallée dans le tissu par la rentrée des cellules nouvelles'. This applies to areolar connective tissue, tendons, and aponeuroses. Cartilage and bone are not susceptible of 'revivification', though the former may be sometimes invaded by fibroblasts which under the influence of the dead graft become transformed into osteoblasts and cells similar to those of bone-marrow, with an ultimate production of bone as in normal ossification from cartilage. C. D. F.

BACTERIOLOGY

Dulaney, Anna D. Non-specific cross-fixation of complement with Wassermann and tuberculosis antigens. *Am. Rev. Tuberc.*, 1922, **6**, 192.

Of 600 cases examined, 100 were tuberculous, and 500 were persons whose blood was examined by the Wassermann test in ordinary hospital routine. The questions asked were: do tuberculous, non-syphilitic sera give positive Wassermann reactions, and do Wassermann-positive, non-tuberculous sera give positive tuberculous fixations? It was found that 8 of the 100 sera from tuberculous patients with neither a history nor clinical evidence of syphilis gave a positive Wassermann with cholesterinized antigen. Of these, 2 sera gave a 1 + fixation with alcoholic antigen. The others were negative. Of the 500 sera received for routine Wassermann tests, 23 giving a positive Wassermann also gave fixations with tuberculosis antigen, while 20 Wassermann-negative sera gave positive tuberculosis complement fixations. The 23 sera, giving fixations with both Wassermann and tuberculosis antigens, represented 3 active and 2 suspect cases of tuberculosis, 15 cases with no anamnestic or clinical evidence of tuberculosis, and 3 cases without any histories. Of the 20 sera giving negative Wassermann but positive tuberculosis complement fixations, 7 were from cases of active tuberculosis, 5 from suspected or treated cases of syphilis without evidence of tuberculosis, 7 from persons without any sign of tuberculosis, and 1 from a case without a history. The conclusion is drawn that a positive tuberculosis complement fixation indicates active tuberculosis in the great majority of cases. The sera of definitely tuberculous cases, which give a positive Wassermann without any other evidence of syphilis, should be regarded as instances of non-specific cross-fixation. When only a cholesterinized antigen is used, a positive Wassermann in active tuberculosis should not be accepted without thorough investigation. C. L.

YABE, S. The leucopenia after the inoculation of influenza vaccine into the human body. *Kitasato Arch. of Exper. M.*, 1922, **5**, 79.

After inoculation with a vaccine made from *B. influenzae*, Yabe found a leucopenia in all cases where the inoculated individuals had not previously had influenza. The diminution in the number of leucocytes lasted for a week. At first all the different leucocytes were involved, but recovery to the normal took place quicker with the lymphocytes than with the neutrophils. The inoculation of influenza vaccine in persons who had contracted influenza a year previously resulted in the same leucocytic changes, the author inferring from this that immunity from influenza does not persist for a year. When a second dose of vaccine was given in the period of immunity resulting from a first dose the leucocytes were increased and then diminished, but in a degree which is less than the leucopenia following a first dose. A similar result was obtained when persons were vaccinated one or two months after contracting natural influenza. If the vaccine was administered when the fever had just subsided the leucopenia was the usual result. From the study of the course of the leucocyte curve the author considered that influenza vaccination causes the same changes as the naturally acquired disease. W. B.

DAHL, E. Widal's leverpröver og leukocyttallets svingninger. [**Widal's liver tests and the oscillations in the number of the leucocytes.**] *Norsk Mag. f. Lægevidensk.*, 1922, **83**, 782.

Dahl has tested Widal's claim that hepatic insufficiency can be demonstrated by exploiting the haemoclasic crisis, the chief features of which are leucopenia, a fall of blood-pressure, and an increase of the coagulability of the blood. Dahl chose 72 patients at random, and 50 were examined in accordance with Widal's prescription, the remaining 22 being kept fasting throughout the tests. The patients were classified according as the number of the leucocytes showed an increase, a decrease, or irregular variations. Cases of liver diseases were found in all three classes, and leucopenia was observed in patients with healthy livers as well as in more than 50 per cent. of the fasting patients. Dahl concludes that Widal's 'digestive haemoclasia' is of no practical value in testing the functional activity of the liver, and he finds that the number of the leucocytes in the capillaries is not constant from minute to minute even in fasting persons kept absolutely quiet. C. L.

v. Gutfeld, F. Ueber die Herstellung, Prüfung und Verwendbarkeit haltbarer Typhus- und Choleraimpfstoffe (Trockenimpfstoffe). **[On the preparation, testing, and application of durable typhoid and cholera vaccine (dry vaccine).]** *Centralbl. f. Bakteriol.* (&c.), Abt. 1, 1922, Orig. **88**, 455.

The author recommends the use of bacteria killed by drying at 37° C. A vaccine prepared in this way was found to be durable and effective.

W. B.

Atkin, E. E., and **Bacot, A.** **Experiments on the infectivity of typhus virus contained in lice (*Pediculus humanus* and *Pedicinus longiceps*).** *Brit. J. Exper. Path.*, 1922, **3**, 196.

A Polish and an Irish strain of typhus virus appeared to be identical as shown by cross-immunity experiments. Guinea-pigs were infected by the injection of the emulsified alimentary tracts of human lice which showed heavy infection with *Rickettsia prowazeki.* Some of these lice had been infected by feeding on typhus-infected monkeys, others by the rectal injection of platelet material obtained by the centrifugalization of blood from infected guinea-pigs. One monkey was infected with typhus by subcutaneous inoculations of infected monkey lice (*Pedicinus longiceps*), and a second was probably infected by the transference of living monkey lice from an infected monkey. Two attempts to infect guinea-pigs by the injection of infected monkey lice failed. Attempts to infect monkeys and a guinea-pig by feeding infected human lice upon them failed. An attempt to infect a guinea-pig with the excreta taken from heavily infected human lice failed.

This paper is the last scientific publication of the late Mr. Bacot.

P. F.

Duval, C. W., and **D'Aunoy, R.** (1). **Studies upon experimental measles. II. The enanthematous, exanthematous, pyrexial, and leucocytic syndrome produced in the rabbit by intravenous inoculation of blood from cases of human measles.** *J. Exper. M.*, 1922, **36**, 231.

Duval, C. W., and **D'Aunoy, R.** (2). **Studies upon experimental measles. III. The symptom complex in the guinea-pig and rabbit following the intratracheal and intravenous injections of filtered nasopharyngeal secretions from cases of human measles.** *J. Exper. M.*, 1922, **36**, 239.

In a previous communication (*Medical Science*, 1922, **6**, 418), the authors reported the successful propagation of the virus of measles in the guinea-pig, the criteria of successful transmission being leucopenia, pyrexia, and nephritis after an incubation period. A definite rash was not seen. In the present communication they refer to experiments in rabbits, injected with the blood of measles, or after passage through rabbits. After an incubation period of 2 to 5 days the animals showed pyrexial, leucocytic, and cutaneous alterations, with coryza and conjunctival injection. Lesions similar to Koplik's spots occurred on the buccal side of the oral cavity. The rash was found to occur between the third and seventh day, and was at first macular and later papular. Passage of the virus through rabbits appeared to exalt the virulence of the virus. Pneumonia was not present in experimental animals. In the second paper the authors describe experiments in which measles was believed to be communicated to guinea-pigs and rabbits from the intratracheal or intravenous injection of filtered nasopharyngeal secretions from cases of measles in man. W. B.

ALESSANDRINI, A. Sulla colorazione delle spore. [**On the staining of spores.**] *Ann. d'ig.*, 1922, **32**, 362.

Smears or sections are stained for two minutes in steaming Ziehl's fuchsin, in which they are left for another 15 or 20 minutes while the stain is allowed to cool. After a thorough wash in running tap-water the specimens are differentiated in 5 per cent. sodium sulphite and then counterstained with a watery solution of methylene blue or malachite green. Dry and mount as usual. The spores remain stained bright red even if the treatment with sodium sulphite is prolonged for more than one hour. Smears must be fixed by passing them over a flame. It is not said how histological material should be fixed. C. D. F.

CHAMBERS, R. New micro-manipulator and methods for the isolation of a single bacterium and the manipulation of living cells. *J. Infect. Dis.*, 1922, **31**, 334.

A modification of Barber's single cell isolation method—but the following advantages are claimed: (*a*) simplicity of construction; (*b*) no lost motion through wear and tear; (*c*) accurate and continuous control of the movements of the pipette in any direction under the highest magnifications; (*d*) maintenance of the tip of the pipette while it is being moved backward and forward in any of the three directions, and (*e*) existence of adjusting devices to facilitate placing the pipette in position. The mechanical details must be consulted in the original paper. W. B.

KAHN, M. C. Chambers's micro-manipulator for the isolation of a single bacterium. *J. Infect. Dis.*, 1922, **31**, 344.

The author emphasizes the value of Chambers's micro-manipulator over the original Barber apparatus, and describes in some detail the actual method of isolation of a single bacterium. W. B.

DI MACCO, G. Ricerche sul comportamento della tensione superficiale nell' agglutinazione. [**Investigations on surface tension in agglutination.**] *Arch. d. sc. biol.*, 1922, **3**, 399.

Living typhoid and paratyphoid B bacilli kept in suspension in an isotonic solution of NaCl for 24 hours at 37° C. remarkably lower its surface tension. Nothing similar is observed if the germs are killed with formalin. The surface tension of a fluid in which, through the addition of a specific serum, agglutination has taken place is sensibly lowered, but not so much as in the fluid residual from the bacteric suspension to which normal serum was added. The smaller diminution of the surface tension in the agglutinating system appears due to the absorption of colloids on the part of the germs used. C. D. F.

AZZI, A. Ricerche sulla fagocitosi del bacillo della tuberculosi. I. Potere fagocitario *in vitro* del sangue di cavia normale e tubercolosa. [**Investigations on phagocytosis of tubercle bacilli. I. Phagocytic power *in vitro* of the blood from normal and tuberculous guinea-pigs.**] *Arch. d. sc. biol.*, 1922, **3**, 379.

Phagocytosis of tubercle bacilli on the part of blood-cells from normal guinea-pigs shows, *in vitro*, small daily differences probably due to experimental errors. The phagocytic power of the blood from tuberculous guinea-pigs decreases as the general conditions of the infected animals become worse. Tubercle bacilli are ingested by polymorphocytes and large mononuclear lymphocytes within which most bacilli remain apparently unaltered. A remarkable positive bacteriotropism on the part of lymphocytes is noticed. C. D. F.

PONTANO, T. Tipi di pneumococchi in Italia. [**Types of pneumococci in Italy.**] *Ann. d'ig.*, 1922, **32**, 525.

Type I of the Rockefeller Institute was isolated from 51 per cent., Type II from 22 per cent., Type III from 11 per cent., Type IV from 4 per cent. of all cases investigated. Type III was found to be the most virulent of all; Type I most frequently gave pleural complications, while articular localizations were due to Types III and I; Type IV was obtained from a case of primary diplococcic meningitis. C. D. F.

GOSIO, B. Ricerche batteriologiche sull' influenza. Introduzione. [**Bacteriological investigations on influenza. Introduction.**] *Ann. d'ig.*, 1922, **32**, 1.

GOSIO, B., e MISSIROLI, A. Ricerche sul potere tossigeno del bacillo di Pfeiffer, in rapporto alla patogenesi dell' influenza. [**Investigation on the toxic power of *Pfeiffer's bacillus* in relation to the pathogenesis of influenza.**] *Ann. d'ig.*, 1922, **32**, 6.

CALDAROLA, P. Terreni nutritivi idonei alla coltura del bacillo di Pfeiffer. [**Culture media for the development of *Pfeiffer's bacillus*.**] *Ann. d'ig.*, 1922, **32**, 27.

ZANNELLI, P. Contributo all' identificazione del bacillo di Pfeiffer. [**On the identification of *Pfeiffer's bacillus*.**] *Ann. d'ig.*, 1922, **32**, 38.

SANTANGELO, G. Sulle alterazioni istopatologiche prodotte dal bacillo di Pfeiffer. [**Histopathological lesions due to Pfeiffer's bacillus.**] *Ann. d'ig.*, 1922, **22**, 45.

GOSIO, B. Sulla preparazione di un siero antiinfluenzale. [**On the preparation of an anti-influenzal serum.**] *Ann. d'ig.*, 1922, **32**, 58.

GHIRON, M. Sieroterapia specifica dell' influenza. [**Specific serotherapy of influenza.**] *Ann. d'ig.*, 1922, **32**, 65.

CALDAROLA, P. Polmonite sperimentale da simbiosi batteriche. Contributo alla patogenesi dell' influenza. [**Experimental pneumonia from bacteric symbioses. Contribution to the pathogenesis of influenza.**] *Ann. d'ig.*, 1922, **32**, 74.

GOSIO, B. Considerazioni riassuntive. [**Considerations and summary.**] *Ann. d'ig.*, 1922, **32**, 82.

The present papers are the outcome of a set of investigations carried out under the direction of Gosio, in the bacteriological laboratories of Public Health, in Rome. The research extended over a period of more than three years, and dealt with all the principal questions connected with the aetiology of influenza. The following conclusions are particularly worth mentioning: The haemophilia of *B. influenzae* is specific, viz. subordinated to the presence in the culture media of substances apparently contained in the blood of certain animals such as the pigeon, dove, lapwing, frog, and snake. The blood of other animals (guinea-pig, dog, pig, horse, tortoise, sparrow, rabbit, and man) more or less prevents the development of typical strains of *B. influenzae.* Even under the best conditions cultures of typical strains die out in a short time, averaging from three days to about a week. The typical strains do not ferment arbutin, mannose, lactose, saccharose, and very little galactose and maltose. But they cause an abundant and constant fermentation of glucose and laevulose. In experimental animals (guinea-pigs) it is practically a matter of indifference whether *B. influenzae* is inoculated alive or dead, the lesions it causes being due to its toxicity and proportionate to the dose used. If this is a fatal one the animals die with lesions characterized, in the main, by an intense congestion of all internal organs, but particularly of the lungs, kidneys, and lymph glands, where infarcts and a 'sub-inflammatory' condition are frequently observed. In man the behaviour of the micro-organism is different, probably because of microbic associations without which it would not perhaps proliferate and become so highly toxic. In fact, an experimental pneumonia can be obtained in rabbits by inoculating into their air-passages cultures of *B. influenzae* in symbiosis with streptococcus or diplococcus, while no lesion of the kind is observed if a double dose of each of the three germs is inoculated by itself. In the organism of experimental animals *B. influenzae* shows an intense leucotropism. The consequent leucocytosis and phagocytosis may save the animals if the dose inoculated is small; but if it is a large one or if the strain used is particularly toxic, the leucocytosis becomes a means of diffusion of the germs and their toxins. Also in patients affected with influenza a hyperleucocytosis is a symptom of extreme gravity and generally precedes a fatal collapse of the patient's power of resistance. The sero- and vaccinotherapy of influenza have as yet been tried on too small a scale for the expression of any definite conclusion. C. D. F.

Torrey, J. C., and Buckell, G. T. A serological study of the gonococcus group. *J. Immunol.*, 1922, **7**, 305.

The experimental work recorded here has been carried out to determine whether gonococci may be distributed among a number of fixed immunological types. A series of agglutination tests are recorded, in which 47 strains of gonococci were tested with 8 different immune sera, and it is shown that direct determinations of agglutination are not of any definite value in indicating type relationships between gonococcus strains.

Detailed results of absorption experiments are then recorded. In this work 77 strains were used. These 77 strains were first tested with one immune serum. A table showing the results is given, an examination of which shows that a high agglutinating titre does not necessarily mean a specific relationship to the serum strain as measured by absorption. Similar results were arrived at by carrying out absorption and agglutinating tests with the same 77 strains and 9 other immune sera. From these results the authors have been able to select certain strains which they consider to be very closely related, as the homologous agglutinins produced by each were absorbed by each. They conclude, however, that this method of examination does not enable the strains to be distributed into a number of distinct serological types sharply separated from one another, but that there would seem to be one large basal group the members of which are closely related but not identical from an antigenic standpoint. To this main group they refer 39 of the 77 strains examined. This group the authors term ‘ regular’. Bordering on this main group they place 16 strains which show close relationship to some of the main group, but which they consider to be more specialized as regards their antigenic elements. This group they term ‘ intermediate’. The remaining 19 strains showed antigenic variations to a marked degree. These they term ‘ irregular’.

Further experiments are then described with 12 gonococcus strains tested against 27 monovalent sera. Tables of these results show a marked diversity in the range of absorptive capacity of these selected strains.

Thirteen gonococcus strains obtained from cases of vulvo-vaginitis in young girls were then tested with two immune sera prepared from vulvo-vaginitis strains. These sera were also tested with adult strains and the infant strains were tested with adult strain serum. The results indicate that no definite serological distinction can be drawn between infant and adult strains. Complement-fixation tests are then recorded, using as antigens a number of different strains or specially selected strains which from the absorption tests above appeared to be ‘regular’ and to cover a wide range. The conclusion is drawn that on the average better results are obtained by using as an antigen a strain selected as having markedly generalized antigenic affinities than by using a combination of ten strains taken at random. It appears, however, that no one antigen has at present been found to give uniformly satisfactory results. G. T. W.

Tulloch, W. J. Serological examination of one hundred strains of the gonococcus. *J. Path. & Bacteriol.*, 1922, **25**, 346.

The author has undertaken the serological investigation of 100 strains of the gonococcus, to attempt first to determine the probable importance of ‘ strain ’ in vaccine therapy in gonorrhoea, and, secondly, to prepare the way for satisfactorily conducting complement-fixation or other serological tests for the diagnosis of chronic gonorrhoea.

The agglutinating sera used in this investigation were prepared from rabbits. The technique employed was 1. In agglutination, to take a serum with a titre of not less than 1/1600 and so dilute it that on adding an equal bulk of suspension of the organism to be agglutinated the strength of the serum was eight times, four times, thrice, and twice the titre of the serum when tested against its homologue; this is termed ‘8 T’, ‘4 T’, ‘3 T’, and ‘2 T’. The suspensions of organisms used contained 4,000 million cocci per c.cm.

2. In absorption of agglutinins, a suspension was used containing 8,000 million cocci per c.cm., and there was added to this sufficient serum to make the concentration equal to ‘16 T’. After describing some preliminary tests the author details the results obtained from two series of 50 strains. These 50 strains were tested with a serum No. 1887 (called Type I) which from previous experiments appeared to be the least specific of the sera available. Of these 50 strains 31 appear to the author to be closely related in that they all markedly reduce the titre of the test serum. Five further strains reduced the titre of the test serum to a marked degree, but varied considerably in their agglutinative and absorptive capacities. He is of opinion, however, that they must be classed as members of the same group. One other strain which almost completely removed the agglutinins from the test serum, but failed in agglutination, is placed in this group.

Of the remaining 13 strains only two showed any absorptive capacity in respect to the test serum. These 13 strains have been tested with four other sera and by this means 11 are placed and two remain unplaced.

In the second series of 50 strains tested in a similar way, 35 are grouped as Type I, and the remaining 15 are related to the other test sera or are unplaced.

The author concludes, therefore, that 72 per cent. of cases of acute and subacute gonorrhoea in the male are caused by one fairly clearly defined serological type of the gonococcus. G. T. W.

Torrey, J. C., and **Buckell, G. T.** (1). **Cultural methods for the gonococcus.** *J. Infect. Dis.*, 1922, **31**, 125.

Torrey, J. C., Wilson, M. A., and **Buckell, G. T.** (2). **Comparative value, from standpoint of public health, of smears, cultures, and complement fixation in the diagnosis of chronic gonorrhoea in women.** *J. Infect. Dis.*, 1922, **31**, 148.

1. The authors commence their paper by describing in detail the preparation of three media which they have used: *A*. Ascitic-veal-urine-glycerol-peptone agar; *B*. Ascitic-salt free 1·5 per cent. peptone 'vitamin' agar; *C*. A semi-solid agar with a growth-accessory element.

The growth-accessory element in *B* and *C* is supplied by chopped bullock's heart, which is used instead of veal, and is reinforced by a whole egg. Medium *C* is used either with or without the addition of ascitic fluid. In all cases the ascitic fluid is added just before pouring plates or sloping tubes. Using these media the influence of varying hydrogen-ion concentrations has been tested. The conclusion is reached that the optimum reaction is between P_H 6·8 and 7·4, and that variation on the acid side of neutrality is not so detrimental to the gonococcus as variation on the alkaline side. Viability tests show that on a medium with a reaction P_H 6·3–7·4 cultures will frequently survive for several months without subculturing.

The influence of the presence of amino-acids was then investigated. Preparations from liver, casein, and beef were used. It was not found, however, that media, usually rich in amino-acids, produced a greater or quicker growth than those media in which peptone was used in a 1·5 per cent. concentration.

With regard to growth-stimulating substances the authors consider that fresh bullock's heart fortified by a whole egg supplies what is necessary. They find that this factor is not appreciably impaired by boiling for ten minutes, but it is greatly impaired by autoclaving to 120° C. for 30 minutes. The growth-accessory factors are readily absorbed by filtering through flannel or cotton.

Abundant moisture is stated to be a point of prime importance in the growth of the gonococcus, especially in primary growths. Reduced oxygen concentration is said to be of small importance.

Various dyes have been tested with a view to obtaining a selective medium. The success of this, however, does not appear to be very marked. On the question of fermentation tests the authors conclude from their experiments that they constitute the most valuable single criterion for the differentiation of gonococci from other similar Gram-negative cocci. Out of 86 strains tested, none split maltose and 85 fermented glucose. None fermented laevulose or galactose.

2. This paper records the results which have been obtained in the

diagnosis of chronic gonorrhoea in women by cultural methods, and compares the relative value of such methods to smears and complement-fixation tests.

Specimens were collected on swabs which were placed in a semi-solid agar medium for transference to the laboratory. Here four plates were inoculated. These plates consisted of *A* and *B* media described in the previous paper with and without the addition of the dyes methyl violet and iodine green. Cases to the number of 102 were examined, and 29 proved positive. A table of these 29 results is given showing that the medium *A* with iodine green gives the highest number of positive results. The difference between this and medium *B* without the dye is not very striking.

The authors note that the number of viable gonococci as shown by cultures does not necessarily agree with the clinical picture.

A table showing the comparative results of cultures and smears from the same cases shows that in 96 cases cultures are positive in 26, while smears are positive in 13 and suspicious in 17. A comparison of complement-fixation methods with those of smears and cultures shows the methods to be of equal value in subacute cases, but in chronic cases the complement-fixation tests give the highest number of positive results; it would seem, however, that a positive fixation might be obtained for a short period after the infection has been eliminated.

The authors, in their discussion, agree that neither method is of such value that it can be used to the exclusion of the other, and that the cultural technique as carried out by them is not easily applicable to the ordinary clinic unattached to a laboratory. G. T. W.

Moersch, F. P. Actinomycosis of the central nervous system. *Arch. Neurol. & Psych.*, 1922, **7**, 745.

Actinomycotic involvement of the central nervous system is not rare. The process is usually secondary to some other focus in the body and apparently the meningeal type, in which the infection takes place by contiguity, is most frequent. The course of the disease is chronic with markedly insidious onset, meningeal involvement occurring without any clinical sign. The examination of the spinal fluid usually shows a pleocytosis before any clinical symptom of meningitis. A positive result on spinal fluid examination with only slight signs of meningitis is almost pathognomonic. During the terminal stage the diagnosis is certain, but in the early stages a positive diagnosis on clinical symptoms alone is practically impossible. The presence of a chronic phlegmon of the head or neck indicates the possibility of actinomycosis, and an examination of the spinal fluid and a search for sulphur granules should be made. C. D. F.

Smeeton, M. A. The serum ring reaction in tuberculosis. [B.] *Am. Rev. Tuberc.*, 1922, **6**, 588.

Krumwiede's and Valentine's test for the rapid determination of the pneumococcus types consists in extracting the soluble antigen from the sputum and floating the resulting liquid on the top of a small quantity of each of the three types of antipneumococcic serum. A definite contact ring appears at the junction of the two liquids in the tube containing the homologous serum. Since the reaction is presumably one of antigen and antibody, it was tested by Smeeton in the diagnosis of tuberculosis. After examining 150 human sera, he came to the conclusion that while the reaction is more frequent in tuberculous than in normal persons, it is not specific. It does not indicate the degree of immunity of the individual, and is therefore of no prognostic value. C. L.

Gloyne, S. R. Buccal infection with *B. tuberculosis*. [**B.**] *Tubercle*, 1922, **3**, 497–9.

Gloyne has attempted to find answers to the three questions: 1. Are virulent tubercle bacilli commonly present in the mouths of patients suffering from pulmonary tuberculosis? 2. If so, can these organisms be transferred to table utensils? 3. Does the washing of these utensils destroy the bacilli? The mouth-washes of 20 sputum-positive cases were injected into guinea-pigs, and positive results were obtained in 10 cases, in 8 of which the patient had profuse expectoration. Six of the spoons used by the 20 patients also gave positive guinea-pig results; all the 6 patients had profuse expectoration. Other table utensils were not found to be infected. Similar investigations of tea-cups and ward crockery washed in plain water were made, and the results were invariably negative. Hence the conclusion that plain water, if used in sufficient quantity, appears to be a satisfactory sterilizing agent. C. L.

Kirchener, M. Experimentelles zur Prüfung der Frage, inwieweit der Lupus auf humaner oder boviner Infektion beruht. [**Experimental investigation of the question whether lupus is due to infection with the human or bovine type.**] *Ztschr. f. Tuberk.*, 1922, **36**, 482.

At the 'Robert Koch' Institute, Kirchener received 46 samples of lupus tissue for examination between January 1920 and August 1921. For various reasons 10 of these samples were unsatisfactory. Of the remaining 36, 13 gave a negative result when injected into guinea-pigs. The remaining 23 provoked tuberculosis in guinea-pigs, and the germ was found to belong to the human type in 11 cases and to the bovine type in 12. These results tally approximately with those of the English Tuberculosis Commission, but they differ considerably from those of other German investigators who have found the human type far more frequently than the bovine type in lupus tissue.

In an appendix to this paper there is a report of a discussion in the German Lupus Commission. Professor Zieler, of Würzburg, stated that the incidence of lupus in Germany coincided with that of pulmonary tuberculosis, but not with that of bovine tuberculosis. Lydia Rabinowitsch-Kempner reported on 23 cases of lupus. Excised material had been examined directly and by animal inoculation (chiefly guinea-pigs, 2 rabbits). In 2 cases tubercle bacilli were cultivated directly without passage through animals. In 5 cases no live virulent tubercle bacilli could be demonstrated. In 12 cases the bacilli were identified with the human type, in 3 with the bovine type, and in 3 cases the bacilli were typical of neither. While Kirchener holds that the human and bovine types are permanently immutable, Rabinowitsch-Kempner believes in the possibility of a very gradual conversion of the bovine into the human type in the human body. C. L.

Piccininni, F. (1). Il contagio della peste alla luce di un recente episodio di peste in Italia. [**On transmission of plague.**] *Ann. d'ig.*, 1922, **32**, 264.

Piccininni, F. (2). La difficoltà della diagnosi batteriologica della peste in alcuni casi d'eccezione. [**Difficulty of bacteriological diagnosis of plague in exceptional cases.**] *Ann. d'ig.*, 1922, **32**, 277.

1. Observations were made during a small epidemic of plague which occurred between July and September 1921 in the province of Naples. The infection was brought into Naples by rats on ships coming from infected countries, though all possible measures had been taken to prevent the passage of rats from ship to land. Most of the rats caught in the areas where the epidemic was observed were immune against plague. In some of the human cases the disease was transmitted through the flour and corn obtained from mills and storehouses where infected rats were found.

2. In slight forms of plague the biological test alone seldom leads to definite conclusions; it is therefore imperative to have resort to cultures and to the isolation of the germ. C. D. F.

Hektoen, L., and **Corper, H. J. Effect of injection of active deposit of radium emanation on rabbits.** *J. Infect. Dis.*, 1922, **31**, 305.

The authors carried out experiments on rabbits to determine the effect of intravenous injection of active deposit of radium and emanation on antibody formation and on the organs and leucocytes. The method of application is described. It was found that active deposit of radium is lethal when given intravenously in doses of approximately 8 to 10 millicuries per kilo. In lethal doses the active deposit produced an initial leucocytosis with, finally, a marked diminution in the circulating leucocytes, particularly the polymorphs. This was associated with changes in the liver, lungs, lymph glands, spleen, adrenals, and kidneys, frequently accompanied by capillary haemorrhages. Given intravenously, active deposit in non-lethal doses may have a depressing effect on the formation of lysin, and to less extent on precipitin, for sheep's blood. W. B.

Sarti, C. Sul potere battericida di due nuovi preparati d'argento. [**On the bactericidal power of two new silver preparations.**] *Ann. d'ig.*, 1922, **32**, 536.

Experiments were made with two new silver preparations termed argirine and choleval. The former was obtained by E. Sarti, and the second by Morini, in the Dermosyphilopathic Institute of the University of Modena. One per cent. solutions in distilled water or serum of either of the two preparations when inoculated subcutaneously together with fatal doses of *B. pyocyaneus*, *B. anthracis* or spores of the latter, saved from death the injected animals. No similar effect was observed when the inoculations were made intravenously. These different results are explained by assuming that the bactericidal action of silver preparations *in vivo* is due to tissue changes which would prevent the propagation of the inoculated germs.

C. D. F.

Pietravalle, N. La natura delle reagine luetiche e le principali cause di errore nella reazione di Wassermann. [**Nature of luetic reagins and principal causes of error in Wassermann's test.**] *Ann. d'ig.*, 1922, **32**, 651.

Calcium is remarkably and constantly increased in luetic sera giving a positive Wassermann test, and transforms from negative into positive the Wassermann test of sera to which it is added in minimal quantities. Sera rendered artificially positive by the addition of calcium react positively also when tested with other means used for the identification of luetic sera. In the cerebrospinal fluid of luetics, calcium is likewise increased. The fact that the calcium content of the blood-serum is increased in certain physiological or pathological conditions explains the positive Wassermann test sometimes obtained from non-syphilitic sera. The addition of minute quantities of calcium to blood sera creates a condition favourable to the precipitation of their colloids. These actually precipitate in the presence of those of the antigen which are particularly sensitive to the action of calcium. The precipitation of the colloids of the antigen and the serum reduces the acidity of their mixture, which thus no longer possesses the concentration of H-ions necessary for the production of haemolysis. This explains why certain luetic sera no longer give a positive Wassermann test after inactivation. In fact warming at 37° C. for half an hour may render them alkaline, and diluted sera warmed at 70° C. have a strong alkaline reaction. On the other hand, an excessive acidity of the serum may also alter the results of Wassermann's test. Sera should therefore be neutralized before testing them, and only tubes of neutral glass should be used for carrying out the Wassermann test. C. D. F.

Gouwens, W. E. The meiostagmin reaction. *J. Infect. Dis.*, 1922, **31**, 237.

The meiostagmin reaction was introduced as a simple laboratory procedure for the diagnosis of malignant disease. It is the name given to a phenomenon (*meion*, small; *stasso*, a drop) which involves a lowering of the surface tension during incubation when a diluted serum (containing certain antibodies) is mixed with its specific lipoid-containing antigen. The first work on this reaction was done by Ascoli who determined the surface tension lowering that occurred when an alcoholic extract of typhoid bacilli, properly diluted, was mixed with a diluted typhoid immune serum, in the proportion one part of the former to nine of the latter. The surface tension was determined immediately after mixing, and again after two hours' incubation at 37° C. Normal serum used in the same dilutions as the immune serum and mixed with the same alcoholic antigen, served as a control. Shortly after, Izar wrote on the same subject. He prepared an antigen from the spleen of a syphilitic foetus. Specimens of serum from syphilitic patients were tested with this antigen. Control tests were simultaneously made. No non-syphilitic serum gave an increase greater than one drop. In no case was there an increase of more than 1·5 drops when known syphilitic sera were tested against heterologous antigens. In a third article by Ascoli and Izar the question of adaptability of the reaction to the diagnosis of certain malignant tumours was studied. They used as antigens the ether soluble portion of evaporated alcoholic extracts of microscopically diagnosed tumours. Only a small percentage of the cases examined gave positive reactions. Lastly Izar and Usuelli elaborated very considerably on the details of the various steps in the meiostagmin reaction. Physicians have failed to use this method of diagnosis first advocated by Ascoli and Izar. In view of this, and of the absence of later accurate confirmatory work, the author has set out to determine whether the method is reliable and simple, whether the reaction is specific and if so, does the specificity depend on the presence of lipoidal materials in the antigens employed.

Over 1,100 tests were made, using 200 different mixtures of rabbit serum and antigen. The serum was obtained from animals immunized against *B. paratyphosus* B, and the antigens were prepared from the homologous and several heterologous organisms, and from the liver of a healthy *B. paratyphosus* B immune rabbit. The spontaneous surface tension changes and the limits of experimental error are as great when relatively dilute serum is employed in the test as when the serum is diluted only 1 in 20. Serum more dilute than 1 in 1,000 shows a smaller degree of, and a slower rate of, spontaneous surface tension change than lower dilutions. These facts apply to normal as well as immune sera.

The substance in the antigen-serum mixtures which is responsible for relatively large experimental error is the blood-serum, as measurements on the various other substances, used in these mixtures, gave constant and accurate readings.

The Du Nouy tensiometer was used. It gives readings with the biochemical mixtures employed which are as accurate as those obtainable with the more cumbersome and slow drop weight apparatus. The sources of experimental error are stated by the author to be less than those involved in use of the Traube stalagmometer.

The meiostagmin reaction does not reveal the presence of antibodies in *B. paratyphosus* B immune rabbit serum of higher titre regardless of the dilutions in which the sera and antigens are used, and of the solvents employed in the preparation of the antigens. W. A. M. S.

BIOCHEMISTRY

Bell, M., and **Mendel, L. B. The distribution of vitamin B in the wheat kernel.** *Am. J. Physiol.*, 1922, **62**, 145.

Wheat contains the water-soluble vitamin B but, compared with other food materials, in relatively small amount. The distribution of the vitamin B is not confined to the embryo, as some authors maintain, but it exists also in the endosperm.

The different milling products of one lot of winter wheat were compared with reference to their content in vitamin B. The results show that the highly milled high grade flours which are used generally for human consumption contain little or no vitamin B, while the low grade flours and bran, which are used as animal foods, are relatively rich in vitamin B. W. C.

Funk, C., and **Paton, J. B. Studies on vitamines B and D.** *J. Metabol. Res.*, 1922, **1**, 737.

There is slight evidence that with diminished food intake, symptoms of beri-beri are delayed on a diet free from vitamin B. Autoclaving for three hours at 25 lb. pressure destroyed vitamin B but had less action on vitamin D. Contrary to existing opinion, growth of yeast takes vitamin D out of solution but leaves vitamin B behind and this method cannot be used for the elimination of the latter from the mixture. C. G. L. W.

Göthlin, G. Fr. Ein Ausweg bei bekanntem Kalorienbedarf eine obere Grenze für den Eiweissbedarf in der menschlichen Kost anzugeben. [**A device to find an upper limit for the protein requirement of man when the caloric requirements are known.**] *Skand. Arch. f. Physiol.*, 1922, **42**, 226.

As the result of an ingenious argument which need not be detailed here, the author arrives at the conclusion that the protein requirement of the average normal man living on a mixed diet is amply covered if he receives 8·8 per cent. of his total intake in calories in the form of protein. Thus for a man leading a sedentary life with an intake of 2,600 calories per day the protein requirement does not exceed 53 gm. protein = 8·3 gm. nitrogen. For a man doing muscular work the protein requirement does not exceed 61 gm. protein = 9·6 nitrogen. Reference to the literature shows that these figures are justified. They are a little more than half of those given by Voit and by Rubner. W. C.

Utheim, K. Advanced chronic nutritional disturbances in infancy. *J. Metabol. Res.*, 1922, **1**, 803.

This very extensive article on nutritional disturbances in infants gives a full review of the work which has been done up to the present and details of the experiments on the protein concentration of blood-serum, the blood circulation, on blood-pressure, the oxidizing function of the body, the caloric-nitrogen and carbon-nitrogen ratios in the urine of athreptic infants, on the creatinine, uric acid and amino-acid excretion, on the organic acids, on the absorption of food from the intestinal tract, on the blood salts, and finishes with estimates of the total metabolism of infants suffering from nutritional disorders. The literature on the subject is very critically reviewed. The author believes that faulty feeding is the main factor in the aetiology of athrepsia and that a quantitative and especially a qualitative starvation is responsible for the development of most cases. The infants who have been followed after treatment in the hospitals have developed into normal individuals. It is also believed that parenteral infection is an important contributing factor in lowering the vitality of artificially fed infants and renders them less able to thrive on artificial feeding. Stagnation of the gastric and upper intestinal contents takes place. A *B. coli* invasion follows and the nutritional disturbance is initiated. The pathogenesis of athrepsia can be considered as a negative energy balance due to insufficient absorption of food from the gastro-intestinal tract, and a decrease in the blood-volume and volume flow of the blood is also believed to be an important factor in maintaining the condition once it has developed. There is a greatly increased loss of food material in the stools during the severe stages of athrepsia, and this loss may be as much as 26 per cent. of the food intake. The loss seems mostly due to the low absorption of fat. Nitrogen retention is either negative or lower than normal in most cases and is also accompanied by loss of sodium chloride and calcium. The main features in the pathogenesis of athrepsia develop naturally one from the

other. The diminished flow of the blood lowers the metabolism causing excretion of unmetabolized constituents in the urine and consequent deficient utilization of food, particularly of nitrogen, with secondary disturbances in salt metabolism. The relatively high heat output indicates that these infants have a high caloric need: 70 to 100 calories per kilo of body weight, which would be sufficient for a normal infant, is insufficient in these cases. Their sugar tolerance is higher than that of normal infants. Hence the feeding must be of high caloric value. This is accomplished by adding easily digested carbohydrate to the whole lactic acid milk feeding. It is noticeable that the majority of the cases give a history of having been fed with sweetened condensed milk, and when this milk is diluted with 12 parts of water there is a feeding which contains much sugar, very little fat, protein and salts, and it is believed that this badly balanced type of food plays a considerable part in the aetiology of many cases of athrepsia. A bibliography of 165 references is appended.
C. G. L. W.

McClendon, J. F. Calcium phosphate metabolism in the diagnosis of rickets. *Am. J. Physiol.*, 1922, **61**, 373.

It is now known that rickets can be produced experimentally by establishing a disproportion between the calcium and the phosphoric acid intake. According to the author a low phosphoric acid intake leads to rickets, a low calcium intake to osteoporosis. From analyses of the skeleton and more skeletal parts of rats, and from metabolism experiments, the author has empirically arrived at a formula by which the diagnosis of rickets can be made. This formula, which he calls the rachitic index, is as follows: determine the average daily increase in weight during a metabolism period and multiply it by 2·2. From this product subtract the daily P retention minus 2 (= the 'corrected' daily P retention). If the rachitic index is negative the animal is normal or it may be osteoporotic; if it is positive the animal has rickets.
W. C.

Underhill, F. P., Tilestone, W., and **Bogert, J. Metabolism studies in tetany.** *J. Metabol. Res.*, 1922, **1**, 723.

Very complete metabolism experiments, especially with regard to calcium, in a fatal case of tetany of intestinal origin. The results were compared with those obtained at the same time on a male and a female subject. There appears to be a much greater tendency for calcium storage in a tetany case than in normal subjects. Very little calcium is eliminated by way of the urine either on a calcium-poor or calcium-rich diet, and change in the calcium intake affects very little, if at all, the amount of calcium excreted by the kidney. In spite of diarrhoea and progressive loss of weight the patient was in positive nitrogen balance and the utilization of protein was excellent. Fat utilization was poor. An attempt to isolate guanidine from the urine failed.
C. G. L. W.

Aub, J. C., Forman, J., and **Bright, E. M. The effect of adrenalectomy upon the total metabolism of the cat. The metabolic effect of adrenalectomy upon the urethanized cat.** *Am. J. Physiol.*, 1922, **61**, 326, 349.

Recent experimental work has had the tendency to belittle the importance of the adrenal medulla and to emphasize that of the adrenal cortex. The evidence presented in these two papers disproves this view. It is shown that after removal of the adrenal in cats there is in addition to muscular weakness a progressive diminution in metabolism which averages 25 per cent. This effect is shown to be due to the absence of the medulla and not of the cortex. Thus, for instance, injection of adrenalin causes a distinct rise in metabolism after adrenalectomy, extracts of adrenal cortex have no obvious effect.

This drop in metabolism occurs in the absence of the thyroid gland. The two glands have similar effects in kind on metabolism, but they produce this effect independently of each other.

Reference is made to several cases of Addison's disease recently reported in the literature where a fall in basal metabolism was observed. W. C.

Marine, D., and **Baumann, E. J. Influence of glands with internal secretions on the respiratory exchange. V. Further observations on the effect of suprarenal insufficiency (by removal) in thyroidectomized rabbits.** *J. Metabol. Res.*, 1922, **1**, 777.

The experiments recorded furnish evidence that a thyroid-suprarenal cortex inter-relationship exists which is separate from the thyroid-chromophil tissue relationship. It appears that the cortex exercises an inhibitory control over thyroid activity, and when the control is removed the thyroid responds with increased activity resulting in increased heat production if a sufficient amount of the iodine containing hormone is liberated. With suprarenal insufficiency there is a rapid loss of iodine from the thyroid. These observations throw light on the thyroid-sex-gland inter-relationship and probably have an important bearing on the aetiology of simple goitre and of exophthalmic goitre. C. G. L. W.

Banting, F. G., Best, C. H., Collip, J. B., Macleod, J. J. R., and **Noble, E. C. The effect of pancreatic extract (insulin) on normal rabbits.** *Am. J. Physiol.*, 1922, **62**, 162.

Hepburn, J., and **Latchford, J. K. Effect of insulin (pancreatic extract) on the sugar consumption of the isolated surviving rabbit heart.** *Am. J. Physiol.*, 1922, **62**, 177.

The name 'insulin' is given to purified alcoholic extracts of pancreas. These extracts have the power to reduce the blood-sugar in depancreatized dogs and in cases of diabetes in man. The present observations on rabbits show that they rapidly reduce the blood-sugar in the normal organism. A dose of insulin which reduces the blood-sugar within four hours to 0·045 per cent. (the normal blood-sugar level being about 0·12 to 0·14 per cent.) is decidedly active in lowering the blood-sugar in diabetic patients. It is possible, therefore, to subject insulin to a physiological assay. A 'unit' is the number of cubic centimetres which in a rabbit causes the blood-sugar to fall to 0·045 per cent. within four hours. The fall of blood-sugar is accompanied by characteristic symptoms of which the earliest are signs of hunger and thirst, hyperexcitability, and apparent fear. Later convulsive seizures may supervene. These symptoms are rapidly counteracted by subcutaneous injections of dextrose.

In the second paper it is shown that insulin when added to the perfusion fluid of an isolated heating rabbit's heart greatly increases the consumption of sugar (from 0·87 mgm. per hour to 3·06 mgm. per gm. per hour). The power of insulin to reduce the blood-sugar is therefore due to a stimulation of the tissues to an increased sugar consumption. W. C.

Rehberg, P. B., and **Carrier, E. B.** **Studies on the physiology of capillaries. V. Concerning the reaction of the human skin capillaries to venous blood.** *Skand. Arch. f. Physiol.*, 1922, **42**, 250.

The increased blood-flow through an organ during activity is due to the opening of capillaries which were previously closed. This is explained by some as being due to the local stimulus of venous blood and attributed to the disappearance of some hypothetical substance present in arterial blood which keeps the capillaries in a state of contraction. To this view of Krogh's are opposed certain observations and conclusions of Bier and of Zak on the condition of the capillaries in stasis. These last-named authors hold that venous blood causes contraction. In the present paper from Krogh's laboratory the experiments of Bier and of Zak have been repeated and their conclusion subjected to a critical discussion. It is concluded that venous blood does not cause contraction of the capillaries; on the contrary, the longer the stasis lasts the more relaxed the capillaries become. W. C.

Drinker, C. K., Drinker, K. R., and **Lund, C. C.** **The circulation in the mammalian bone-marrow, with special reference to the factors concerned in the movement of red blood-cells from the bone-marrow into the circulating blood as disclosed by perfusion of the tibia of the dog and by injections of the bone-marrow in the rabbit and cat.** [**B.**] *Am. J. Physiol.*, 1922, **62**, 1.

In this extensive investigation the functional activity of the bone-marrow has been studied by the method of perfusion and injection. The paper, which is illustrated by a number of instructive drawings, will repay careful study. The main conclusions arrived at are as follows: the capillaries conducting blood in the bone-marrow of the mammal in a condition of normal blood formation are closed structures, lined throughout with epithelium, and not in communication with the marrow parenchyma. When there is a very active red blood-cell formation, the delicate walls of these capillaries are grown through by irregularly placed red cells in varying stages of maturity. The capillaries thus become, for a period of varying length, open structures. But the opening presented does not result in flooding the marrow parenchyma with blood because of the dense packing of the immature blood-cells, which is an essential phase in process of encroachment upon the capillary wall. The stimulus causing growth of red blood forming tissue is thus responsible for the delivery of the red blood-cells to the circulation. W. C.

Gattner, J., u. **Schlesinger, E.** Die Bestimmung der okkulten Blutungen durch quantitative Methoden. [**The quantitative measurement of occult bleeding.**] *Ztschr. f. klin. Med.*, 1922, **94**, 426.

By using progressive dilutions of the faeces and a modification of the benzidine test it is possible to obtain semi-quantitative estimations of the amount of blood present in the stools. The method has the advantage that one is not concerned with the sensitiveness of the reagent used and may form a judgement as to the course of an occult intestinal haemorrhage.

C. G. L. W.

Forbes, A., and **Miller, R. H. The effect of ether anaesthesia on afferent paths in the decerebrate animal.** *Am. J. Physiol.*, 1922, **62**, 93.

Crile has stated that 'ether anaesthesia offers no protection to the brain-cells against the effect of trauma, and that the lipoid solvent anaesthetics probably break the arc which maintains consciousness beyond the brain-cells somewhere in the efferent path'. The present paper disproves this view, by directly observing the electrical changes in the brain when nerve impulses are sent in. Ether is of great value in protecting the brain from such damage as may be done by afferent impulses. The observations confirm Sherrington's view that the synapse is the point at which the effect of the anaesthetic occurs. W. C.

RADIOLOGY

Radiotechnique

March, A., Staunig, K., and **Fritz, O. A spectrometer contrived for the purposes of practical radiology.** *Arch. Radiol. & Electroth.*, 1922, **26**, 285.

The accurate analysis of heterogeneous beams of X-radiation, afforded by the Bragg spectrometer, has led the authors to devise a form of the instrument suitable for practical radiology. The principle of the instrument is based on the fact that, when a pencil of radiation from an X-ray bulb falls upon a crystal, a beam of homogeneous radiation is reflected, the wave-length or hardness of which, for the given crystal, depends only upon the angle at which the original beam strikes the crystal. The reflected beams are of shorter wave-length the more obliquely the initial beam strikes the crystal. In the new instrument the reflected beam impinges on a fluorescent screen, giving rise to a bright line. As the crystal is rotated the bright line moves along the scale of wave-lengths attached to the screen and the brightness of the line varies with its position.

As it has been shown that the wave-length of the hardest rays in an X-ray beam is inversely proportional to the tension on the tube emitting them, the spectrometer serves as an absolute voltmeter and is capable of indicating the voltage applied to a tube to within 500 volts. The authors' researches have shown that the composition (but not the intensity) of the X-ray beam, as regards the distribution of spectral energy, is determined by the wave-length of the hardest ray present. Practically, this distribution of energy is independent of the voltage-time curve of the tube-supply, provided the maximum applied voltage is always the same. Hence it remains to determine the beam of X-radiation most suited to a given radiological problem, when it will be completely specified by the minimum wave-length present. L. H. C.

Coblentz, W. W. Some physical characteristics of the radiation from quartz mercury lamps. *Am. J. Electrotherap. & Radiol.*, 1921, **39**, 395.

The author has devised a method for measuring the intensity of the radiation emitted by quartz mercury vapour lamps, and has used it to determine the decrease in efficiency with use of various types of burner.

The method consists in allowing the radiation to fall upon a bismuth-silver thermopile connected with a sensitive d'Arsonval galvanometer. A quartz cell containing water is interposed between the thermopile and the lamp, to absorb red and infra-red radiations emitted by the hot quartz tube of the latter.

Measurements were made of the total and of the ultra-violet component of the radiation emitted by quartz mercury burners having (1) a solid tungsten, and (2) a liquid mercury anode. The ultra-violet component was determined by subtracting from the galvanometer reading for the total radiation that obtained on transmitting the radiation through a sheet of Corning Noviol glass, which absorbed radiation of wave-length less than $0{\cdot}4\,\mu$. The radiation from each of seven old burners was compared with that from a new one. The data given shows that in the course of a thousand hours the total radiation may decrease to 50 per cent. of that emitted by a new burner.

The magnitude of the ultra-violet component of the radiation from a mercury lamp was found to be independent of the type of anode used. For a new burner the ultra-violet component amounted to 70 per cent. of the total radiation, but decreased to 60 per cent. after several hundreds of hours' use.

The paper contains, in addition, the following interesting data:

1. The variation, with distance from a quartz mercury arc, of the intensity of the emitted radiation is somewhat more rapid than that indicated by the inverse square law.
2. For air-cooled, 110-volt, direct-current burners, the intensity of the light emitted varies as the square of the energy consumed in the burner.
3. By means of a spectro-pyrheliometer, the author has carried out comparative tests on sunlight and mercury vapour radiation. It was found that, at sea-level, the solar radiation of wave-lengths less than $0{\cdot}3\,\mu$ was imperceptible, whereas light of the same wave-lengths from the mercury arc amounted to 5 per cent. of the total radiation. Furthermore, the total ultra-violet radiations from the sun and from a quartz mercury arc (110 volts) at a distance of 30 cm. were roughly the same in intensity.

L. H. C.

Part I. **Levy, Leonard,** and **West, D. W.** *Part II.* **Thorne, Baker, T. The reduction of radiographic exposures to one twenty-fifth of the normal amount by means of a new type of X-ray plate.** *J. Röntg. Soc.*, 1921, **17**, 55.

Part I. The considerable reduction in radiographic exposures is due mainly to optical contact between a photographic film and calcium tungstate. The sensitive emulsion of an X-ray plate is coated with a layer of the fluorescent salt held in a suitable medium, which may be removed by immersing the plate in warm water prior to development. The authors claim that the exposure of the plate may be varied considerably without detriment to the resulting radiograph, which will be free from graininess.

Part II. The author has produced a photographic emulsion which is sensitive to ultra-violet light as short as λ 1900 and in addition possesses absorption maxima corresponding to the emission maxima of the rays emitted by calcium tungstate. This emulsion of itself is suitable for work in the ultra-violet region of the spectrum and the great speed of Dr. Levy's plate is due, in part, to its character. The new plate is found to have properties pertaining to the ordinary X-ray plate, giving the steeper contrast with soft but the greater penetration with hard radiation.

L. H. C.

Radiodiagnosis

Möller, F. Om Roentgenbilledet af interlobære Exudater og Pleurafortykkelser med særligt Henblik paa Differentialdiagnosen overfor tuberkulöse Infiltrater i överste höjre Lap. [**The X-ray picture of interlobar effusions and pleural thickenings, with special reference to the differential diagnosis in tuberculous infiltrations of the right upper lobe.**] *Ugesk. f. Læger.*, 1922, **84**, 1110.

In the course of examining many cases of pulmonary tuberculosis at the X-ray department of the Frederiksberg Hospital in Denmark, Möller has observed 13 in which the X-ray signs were almost precisely those supposed to be pathognomonic of an effusion between the upper and middle lobes of the right lung. In some cases the shadow was, indeed, not quite uniform, but in others it was as uniform as in the case of an interlobar effusion. The clinical signs pointed in every case to tuberculous infiltration of the base of the right upper lobe, and ordinary physical examination and exploratory puncture failed to reveal any interlobar effusion. Tuberculous infiltration, throwing a shadow exactly like that of an interlobar effusion, is evidently quite common. When the lower border of the shadow is sharply defined, the odds are that it is due to infiltration of the lung, rather than to an interlobar effusion. But the reverse is the case when the upper border of the shadow, which is band-shaped or triangular, is sharply defined. A similar shadow may be thrown by a simple broncho-pneumonia of the base of the right upper lobe, and only when all the other evidence, apart from the X-rays, has been taken into account, can the differential diagnosis be satisfactorily settled. C. L.

Dahlstedt, H. Beiträge zur Kenntnis des lokalisierten Pneumothorax bei Lungentuberkulose. [**A contribution to the study of localized pneumothorax in pulmonary tuberculosis.**] *Beitr. z. Klin. d. Tuberk.*, 1922, **52**, 79.

Dahlstedt's paper is a recantation of his earlier opinion that the X-rays alone are sufficient for the diagnosis of cavities in the lungs. In one case the skiagram showed a 6 by 6 cm. annular shadow to the right of the hilum of the right lung. A horizontal line at the base of this shadow remained horizontal on changes of posture. As there were no clinical signs of a cavity, it was assumed that it must be near the centre of the lung. Two months later there was no annular shadow, and its place on the skiagram was taken by some fine lines indicative of thickening of the interlobar pleura. As there was no history in the interval of an encapsuled empyema having burst into the bronchi, a localized, interlobar, spontaneous, sero-pneumothorax was diagnosed. Dahlstedt has recently seen three such cases of a small sero-pneumothorax, throwing an annular shadow strikingly suggestive of a cavity, and during the past two years he has seen at his sanatorium no fewer than 12 cases in which the X-ray diagnosis of a cavity had to be revised, chiefly because the annular shadows, on which this diagnosis depended, disappeared in a few weeks. As there is no X-ray sign which is pathognomonic of a cavity, it is unwise on this evidence alone to recommend heroic measures, such as thoracoplasty, which may be necessary in cavernous phthisis, but are hardly justifiable in such a comparatively trifling lesion as a small, accidental pneumothorax. C. L.

Radiotherapy

Holfelder, H. Die Roentgentiefentherapie der malignen Tumoren und der äusseren Tuberkulose. [**Deep Roentgen-therapy of malignant tumours and of surgical tuberculosis.**] *Strahlentherapie*, 1922, **13**, 438–67.

This paper is divided into three sections, the first dealing with general and technical considerations, the second with special sites and types of malignant growths, and the third with surgical tuberculosis in its different forms. The factors rendering surgical malignant lesions more difficult to deal with than gynaecological are pointed out, and the value in many cases of using a three-field method, converging at angles of 120 degrees, so as to give an approximately quantitative homogeneity, is emphasized (diagrams). Long pauses are recommended between radiations in full doses so as to avoid cumulative effects (late necrosis, &c.), e. g. 8–12 weeks after one irradiation, 12–16 weeks after a second, 6–8 months after a third, and, should a fourth be necessary, then only after 8–12 months should it be administered. Surgical sarcomata should be given at least a 90 per cent. skin-dose throughout, as many of them are less radiosensitive than uterine sarcomata, and better results are gained if radiation treatment alone be carried out, without operation or even a test-excision.

As a routine all operative carcinomata are given a full homogeneous radiation followed, in four weeks by the operation, then in four weeks another radiation of the site, and further radiations as required in periods as above-mentioned. Considering special sites, skin-epitheliomata are the most favourable of all cancers for radiation, hard rays at a distance being used. As many brain-tumours are of low radiosensitiveness, an attempt should be made to deliver 120–130 per cent. to the site of the lesion; this involves cross-fire, small fields, and radiation from a long distance. Maxillary and tonsillary carcinomata also require doses of from 120–130 per cent. skin-dose. For tongue and lower jaw cases and the related glands there is danger of laryngeal damage owing to the transradiant air-space, unless some technique like the author's paraffin-collar method be used, and his three-field irradiation. Thyroid and branchiogenic carcinomata are highly favourable for radiation. Mammary tumours are treated with two tubes at 80–100 cm. distance from the skin, one in front and one behind, each giving 50 per cent. ED., and an additional field above the shoulder-blade from 40–50 cm. In this way the whole area of possible direct extension is covered. Bone-metastases from breast-lesions are considered favourable, at least so far as the results up to the present.

For lung and mediastinal tumours a divided dose method is recommended, half at one time, and in a few weeks the other half, the heart being avoided as much as possible. For oesophagus cancer very high dosage is necessary with a small narrow diaphragm. In stomach-malignancy the use of oblique rays from behind and above obviates over-dosage of the suprarenals, which is a cause of much of the apathy, &c., often observed after gastric irradiations. Liver-metastases have been found frequently to subside with homogeneous radiation, and pancreatic cancer on the whole is found favourable. Sigmoid is more amenable than rectal carcinoma. A useful summary is given of the technique advised in the various sites of surgical tuberculosis. J. H. D. W.

Amundsen, P. Blodundersökelser av radiologer og radiologisk hjälpepersonel. [**Blood examinations of radiologists and their assistants.**] *Tidsskr. f. d. norske Lægefor.*, 1922, **42**, 862.

Since the spring of 1921 examinations have been carried out on the blood of fifteen persons directly or indirectly associated with an X-ray radium institute. The blood was usually drawn between 11 and 12 in the morning, and its haemoglobin content was determined by Sahli's method (80 degrees of Sahli being equivalent to 100 per cent.). The red cells and the leucocytes were counted in a Thoma-Zeiss chamber, and Pappenheim's modification of Grünwald's staining method was used for the differential count. Under the heading 'monocytes' were included the large mononuclear cells and Ehrlich's transitional cells. Without exception the haemoglobin was 100 per cent. or more. The colour index was about the normal. The number of leucocytes was in a few cases somewhat below the normal average, but was never below the lowest limit for the normal. The most remarkable observation was the relative lymphocytosis, the polynuclear leucocytes being scanty relative to the number of the lymphocytes. Even the two servant girls and the night watchman attached to the radium institute showed this change, as did also the photographer who had nothing to do with the rays, and whose only duty at the institute was to take photographs of the patients' ulcers and tumours. It was also remarkable that two medical students, who had done only one month's service at the institute, showed the typical blood-count of the radiologist. One of Amundsen's tables shows the blood records of seven persons whose blood was examined before as well as during their employment at the institute, and this table again shows the capacity of certain rays to provoke a relative lymphocytosis. Another table shows that a holiday from the institute speedily reduced the radiologist's relative lymphocytosis. These investigations suggest that in spite of the usual protectives, such as lead, rubber, and glass, the radiologist is not fully screened, and every one who works with the X-rays and radium should constantly inspect and control his protective gear before it is too late. C. L.

Rechou. Rapport sur la radiothérapie de la tuberculose pulmonaire. [B.] [**Report on the radiotherapy of pulmonary tuberculosis.**] *J. de radiol. et d'électrol.*, 1922, **6**, 425.

The author states that there is not enough material from which to judge exactly how the spleen should be irradiated in pulmonary tuberculosis or to define the indications and contra-indications for such treatment. All new methods must be studied carefully and scientifically to find out their exact merits. The paper is a *résumé* of the latest work on the subject from many sources.

1. *Direct irradiation of the lungs.* In many cases the results seem to have been more harmful than beneficial; in most cases this was because the dose given was too weak, but sometimes bad results followed the application of stronger doses.

2. *Irradiation of the spleen.* The first phenomenon seen is a marked modification of the blood picture, which it is impossible to doubt is due to the irradiation.

A. *The technique of Manoukhine.* Manoukhine has studied the treatment of pulmonary tuberculosis by irradiation of the spleen since 1913, the object being to produce an intense leucocytolysis. Eight thousand cases in all stages have been treated. A cure is only effected after the leucocytolysis which is produced by substances of the class of soluble ferments: a leucocytolysis is produced by different soluble ferments which neutralize the first-named when mixed with them. The former are produced in the spleen, the latter in the liver. The author criticizes Manoukhine's theory very strongly, and states that his method of measuring the dose is useless and inaccurate. The dose used varied, according to the state of the patient, from ½ H–1 H units; this and other points in the technique come in for severe criticism. The results obtained are: Tuberculosis of the first degree, 1,462 cases, all cured; of the second degree, 3,211 cases, 7 deaths; of the third degree 2,406 cases, 54 deaths. In his conclusion the author says, 'these are the facts, ought we to believe them? It is up to us to check them.'

B. *The researches of Verdun and Dausset.* About 30 cases have been treated by irradiation of the spleen: the technique is shortly given. Beneficial results were obtained in 60 per cent. of cases. In those cases which showed good results quickly there was a leucocytosis from 9,000 to 12,000 before treatment, up to 15,000 to 21,000 after irradiation. It is stated that the cases that did well had at first 80 per cent. of polynuclears.

C. *Researches of Trémolières and Colombier.* These are based on the work of Manoukhine; they give a dose of 1 H at the skin. They irradiate the long bones as well as the spleen. The results are stated to be good, and they notice a diminution in the number of the bacilli.

D. *The author's technique and results.* Based on about 100 cases in various stages. Three blood examinations were made in each case, before and after irradiation and at the end of two months, but in all cases these were incomplete. In all except the first five cases the spleen alone was irradiated, in the others the lungs were included. In all cases the liver was screened from the effects of irradiation. The technique used is fully described. If there is a destruction of the red blood corpuscles the irradiations should be stopped. The cases were classified according to the modifications of the blood into (1) those which showed a considerable increase in red cells; (2) those in which the increase was small or absent; (3) those in which the number of red cells decreased. All the cases in Class 1 were benefited by treatment, some absolutely cured. In Class 2 the author considers the benefit to be nil, and in Class 3 the red cells often dropped to 1,000,000 per c.mm., and in all the clinical signs and general condition became worse. Reference is made to the leucocytes in the three classes, from which it appears that they are not affected in a constant manner in any class; as regards the polynuclears the author does not agree with Verdun and Dausset. The cases referred to were 24 in the first class, of which 5 showed particularly good results, 41 in the second class, and 17 in the third class. In all there was a considerable drop in the lymphocytes.

Conclusions. (1) Irradiation of the spleen seems to be able to benefit a certain limited number of cases of pulmonary tubercle. (2) Benefit results when there is an increase in the red blood corpuscles after irradiation. (3) The modification in the leucocytes is very variable in those benefited. (4) The polynuclears vary, the lymphocytes always fall. (5) The method needs further careful study. P. L.-B.

Collin, E. A study on the Roentgen aspect of tuberculosis of the joints and its relation to the clinical aspect, especially when under treatment by universal light baths. *Acta Radiolog.*, 1922, **1**, 395.

After giving a short review of the rather sparse literature on the subject, the author gives the histories, both clinical and X-ray, of 12 cases, with the conclusions drawn from each. A general summary of conclusions is given as follows:

1. Even if the X-ray picture reveals no sign of tuberculosis it does not exclude the possibility of the affection being tuberculous.
2. In some cases the X-ray changes only appear when the clinical symptoms have improved considerably.
3. The light treatment of surgical tuberculosis can yield very good results even when serious changes are found under X-rays: therefore on these alone a bad prognosis should not be given.
4. Complete healing radiologically may occur long after the clinical symptoms have disappeared.
5. Tuberculous osteitis may heal spontaneously: under light treatment the cosmetic result is better and attained more quickly.
6. In some cases clinical improvement is accompanied by deterioration, as seen by X-rays. This is a sign that the diseased material is being absorbed.
7. Extensive arthritis in hand, ankle, knee, and elbow can heal with the new formation of articular cartilage and good function.
8. A joint seen to be deformed under X-rays may show completely free function clinically.

Thirty-six X-ray photographs accompany the paper.

P. L.-B.

Jeanselme et **Barbé**. Étude statistique sur le cas de cancers traités à l'hôpital Senon pendant la période sexennale 1901–6. [**Statistical study of cancer cases during six years (1901–6).**] *Les Néoplasmes*, 1922, Jan. 28.

(1) Out of 86,785 adult patients 1,501 had cancer. (2) Of these 1,501 cases of cancer, 518 (i. e. one in 8·2) were men, and 983 (i. e. one in 4·4) were women.

(3) The percentage of mortality was as follows:
(*a*) Between the ages of 30 and 40, men 4·4 per cent.
,, ,, ,, ,, ,, ,, ,, women 9·17 per cent.
(*b*) ,, ,, ,, ,, 50 ,, 60, men 13·0 per cent.
,, ,, ,, ,, ,, ,, ,, women 28·0 per cent.
(*c*) ,, ,, ,, ,, 60 ,, 70, men 14·0 per cent.
,, ,, ,, ,, ,, ,, ,, women 28·0 per cent.

(4) Of these 1,501 cases of cancer, 409 were attacked in the uterus, 296 in the stomach, and 153 in the breast. (5) The genital organs are attacked 11 times in men and 584 times in women; and the digestive organs 384 times in men and 247 times in women.

(6) There would seem to be no more evidence for attributing any occupational predisposition to cancer than there is for the endemic character of the disease. These data should prove of value when compared with those of subsequent periods—they would help to evaluate in an indirect way the benefits of modern methods of treatment of cancer, e. g. X-rays or radium.

M. B. D.

Radiobiology

Hess, A. F., Unger, L. J., and **Pappenheimer, A. M. I. Experimental rickets in rats. VII. The prevention of rickets by sunlight, by the rays of the mercury vapour lamp, and by the carbon arc lamp.** *J. Exper. M.*, 1922, **36**, 427.

Hess, A. F., Unger, L. J., and **Steiner, J. M. II. Experimental rickets in rats. VIII. The effect of Roentgen-rays.** *J. Exper. M.*, 1922, **36**, 447.

I. Lately it has been shown that the experimental rickets of rats can be favourably influenced by light, as is the case in infantile rickets. The authors have carried out a large series of experiments, using sunlight and other rays under many different conditions. The results are summarized in eight tables published with the paper. As regards sunlight, daily exposures of 15 minutes protected rats fed on a standard ricket-producing diet adequate in its Ca but inadequate in its P: the effect is stated to be equivalent to doubling the phosphorus. The same degree of protection could not be produced in November and December; the authors believe this to be due to a lack of ultra-violet rays at this season. The experiments confirmed the fact that the sun loses its potency after the rays have passed through a glass window. Rays from the mercury vapour-lamp afford marked protection when given in small amounts; with an alternating current of 160 volts, exposures of 3 minutes or less at 3 feet were found sufficient. An attempt was made to protect rats by irradiation before they were placed on the experimental diet, but this did not delay the onset or decrease the intensity of the lesions. According to the authors three factors determine the influence of light—the diet, the rate of growth, and the degree of pigmentation of the skin. A series of experiments regarding the third factor is described. The carbon arc lamp was used in many cases: as its spectrum resembles that of sunlight more closely than does that of the mercury vapour-lamp it was thought that it might be of value in rickets. This was found to be the case both in experimental and infantile rickets. By means of it infantile rickets can be readily cured; in rats a daily exposure of 3 minutes at a distance of 3 feet afforded protection. The carbon arc was also used with more complex diets, which are described, from which the authors conclude that light can compensate to an important degree for a diet deficient in either Ca or P. Temperature was found to have no effect on the protection afforded by light.

In all cases the lesions were examined by X-rays, but the final diagnosis of rickets was made after histological examination. Three X-ray photographs accompany the paper.

II. In this paper the authors tested the protective power of soft X-rays against rickets in rats. Exposures of 15 minutes at 8 inches from the Coolidge, and also 2 minutes at 3 feet, with a $\frac{3}{4}$-inch spark-gap, 15 milliamps, and no filtration, in both cases failed to prevent rickets. The next series of experiments was done on rats receiving a diet just sufficient to prevent rickets to see whether intense X-radiation produced rickets; in no case did rickets develop. The differences in the blood picture between the experimental and control animals under the second experiment are described, the most marked feature being a leucopenia affecting the lymphocytes for the most part.

Four X-ray photographs accompany the paper. P. L.-B.

MEDICAL SCIENCE

ABSTRACTS & REVIEWS

Volume VII. Number 6 March 1923

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In the references the letter [B] after the title signifies that the original memoir contains a good bibliography of the subject dealt with.

REVIEWS

LETHARGIC ENCEPHALITIS

Epidemiology. In his annual report for the year 1921 the chief medical officer of the Ministry of Health shows that there has been a pro-

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a fresh outbreak at the beginning of 1921, but not so extensive or severe as in the previous winter; the disease again became most prevalent between the end of February and beginning of March; the curve then fell as rapidly as it had risen, and only sporadic cases were observed. The total number of cases notified in 1920 was 984, but this figure was undoubtedly incorrect, as encephalitis was not made notifiable in Switzerland till February 17, so that a number of cases were not notified, apart from abortive forms which were not seen by medical men at all or were not recognized as cases of encephalitis. The morbidity was 2·5 cases per 10,000 inhabitants. The disease spread throughout the country, no part being completely spared. Contrary to the rule in transmissible diseases, the large towns did not appear to be affected much more than the rest of the country. The incidence was highest between the ages of 15 and 49. It was slightly higher in men (2·8 per 10,000) than in women (2·5 per 10,000). The deaths amounted to 290 or 29·4 per cent., 162 occurring among males (0·9 per 10,000) and 128 among females (0·6 per 10,000), whereas the Danish statistics show a higher mortality among females. In 1921 only 113 cases were notified in January,

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MEDICAL SCIENCE

NEW EDITORIAL ARRANGEMENT

The Medical Research Council beg to announce that they have made new editorial arrangements for the sections of medicine and surgery in "Medical Science," and that these will become effective as soon as possible during the course of publication of Volume VIII.

It is proposed to subdivide these subjects and to place specialized parts of them under suitable individual editorship. This will be undertaken chiefly by those engaged in research and higher teaching at various medical schools.

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REVIEWS

LETHARGIC ENCEPHALITIS

Epidemiology. In his annual report for the year 1921 the chief medical officer of the Ministry of Health shows that there has been a progressive increase in the number of cases of lethargic encephalitis notified in England and Wales during the last three years, viz. 1,470 in 1921, as compared with 844 in 1920 and 524 in 1919. The case mortality for 1921 was 42·0 per cent. as compared with 49·3 per cent. in 1920. The cases were widespread but scattered, and there was no positive correlation in distribution with poliomyelitis or cerebrospinal fever. 82·3 per cent. of the total cases were in urban districts, including London, and 17·7 per cent. in rural districts; 15·1 per cent. of the total cases were in London. As in preceding years the majority of cases were reported during the first quarter, but the outbreak in January and February 1921 far exceeded the seasonal rise of the two previous years; there was no repetition of the 'summer rise' which was noticed in 1920. It would appear as if the disease had spent its epidemic force during the winter of 1920–21, and there was reason to think that it had become less malignant in its clinical manifestations.

According to Carrière, the Swiss delegate of the Committee of the International Office of Public Health, the first case of epidemic encephalitis observed in Switzerland in recent years was reported by Staehelin, at Basle, in 1917, but it was not until the end of 1919 that the disease became frequent, reaching its height in March 1920, after which it rapidly decreased. By the end of June cases of encephalitis became very rare, and in the second half of the year the disease practically disappeared. There was a fresh outbreak at the beginning of 1921, but not so extensive or severe as in the previous winter; the disease again became most prevalent between the end of February and beginning of March; the curve then fell as rapidly as it had risen, and only sporadic cases were observed. The total number of cases notified in 1920 was 984, but this figure was undoubtedly incorrect, as encephalitis was not made notifiable in Switzerland till February 17, so that a number of cases were not notified, apart from abortive forms which were not seen by medical men at all or were not recognized as cases of encephalitis. The morbidity was 2·5 cases per 10,000 inhabitants. The disease spread throughout the country, no part being completely spared. Contrary to the rule in transmissible diseases, the large towns did not appear to be affected much more than the rest of the country. The incidence was highest between the ages of 15 and 49. It was slightly higher in men (2·8 per 10,000) than in women (2·5 per 10,000). The deaths amounted to 290 or 29·4 per cent., 162 occurring among males (0·9 per 10,000) and 128 among females (0·6 per 10,000), whereas the Danish statistics show a higher mortality among females. In 1921 only 113 cases were notified in January, February, and March as compared with 826 in the first quarter of 1920. The contagiousness of the Swiss cases was very ill marked; with the exception of a few family or house epidemics, the cases were almost always isolated. Epidemic hiccough in Switzerland was first observed in the winter of 1919–20 by Gautier, who regarded it as a form of lethargic encephalitis, though a direct relation with this disease was rarely established.

In a communication to the Committee of the International Office of Public Health, Sterling states that the history of lethargic encephalitis in Poland dates back to the year 1917, when several deaths occurred in different districts during the first few months of the year. The epidemic, however, was not exhaustive or of great severity. Most of the cases were observed at Warsaw, where children and young persons were chiefly affected. The clinical picture corresponded to Economo's description of the cases in the Vienna epidemic and the oculo-lethargic form of French writers. Several incomplete forms were observed. In the great majority of cases complete recovery took place, and there were no relapses or residues of the original disease. An epidemic of encephalitis did not visit Poland again until the end of February and beginning of March 1920, when its extent and gravity were much greater than that of the previous outbreak. The disease was made notifiable in March 1920. Contrary to what took place in Switzerland, the height of the epidemic did not occur in the coldest months of the year, but usually in April, and in certain departments in the spring and summer months. As a general rule the course of the epidemic was not synchronous in the different districts of Poland; in the department of Warsaw, for example, the epidemic was declining, while it was still intense in those of Kielce and Leopol. With the exception of Warsaw, in which the overcrowding was excessive owing to its being an asylum for refugees from the eastern provinces and Soviet Russia, density of population was not responsible for the local gravity of the epidemic. In Warsaw, moreover, the disease was more frequently recognized owing to the large number of competent neurologists, who avoided the errors often made in other districts, such as at Cracow, where the real number of cases was considerably higher than that notified. The result of a questionnaire sent to practitioners throughout Poland showed that in certain regions there were small foci of contagion in houses, families, or districts. Of 1,374 cases notified, 848 were Christians and 526 Jews. This high incidence among the Jews is remarkable, as the proportion of the Jewish population in Poland does not exceed 14 per cent., and is a further evidence of the predisposition of the Jewish race for certain diseases of the nervous system, of which Tay-Sachs's disease and torsion spasm are other examples. The great majority of the deaths occurred in April, i. e. at the height of the epidemic. The mortality was higher in women than in men, and least in children. The immediate causes of death included, in order of frequency, exhaustion of the cardiac muscle, pneumonia of one or both lungs, paralysis of the respiratory muscles, cachexia, and suicide during post-encephalitic psychosis.

According to Pearl, of the School of Hygiene and Public Health of Johns Hopkins University, the case incidence of epidemic encephalitis in 1920 in New York City was nearly five times that in 1919. At the same time the case fatality rate increased from 26 per cent. to 37 per cent. The seasonal incidence as judged by monthly distribution of the cases was significantly different in 1920 from what it was in 1919, there being an increase in the spring of 1920 which was lacking in 1919, and a significant autumn outbreak in 1919 which was absent in 1920.

Further information on the epidemiology of the disease will be found in the Ministry of Health's Report by Parsons, MacNalty, and Perdrau, and in Achard's (1) monograph.

Symptomatology. Sanz (1), of Madrid, who suggests the term 'polymorphous encephalitis' as the most appropriate name for the disease, records a case of two years' duration in a man aged 31, which first assumed the delirious form, then the lethargic, later the paretic, subsequently the neuralgic, and finally the parkinsonian.

Sands, of the Bellevue Hospital, New York, who records three cases of epidemic encephalitis simulating cerebral tumour, in two of which operation was decided upon, but refused, remarks that syphilis alone rivals epidemic encephalitis in producing so many clinical pictures.

Eschbach reports two cases, in youths aged 16 and 18 respectively, which occurred at Bourges in the beginning of 1921 and were remarkable for their *rapidly fatal course.* In the first case, which lasted ten days, an irresistible desire to sleep was the only symptom noticed for six days and was followed by complete loss of muscular power and strabismus. The second case, which lasted only four days, was remarkable for the occurrence of a meningeal reaction with headache and vomiting.

During the recent epidemic of encephalitis Barré and Reys have been struck by the large number of patients who complained of vertigo, loss of equilibrium, and lateropulsion, these symptoms appearing earlier and being more pronounced than the ocular symptoms or the drowsiness. The frequency of these cases induced the writers to describe a *labyrinthine form of epidemic encephalitis* which may occur either in association with other signs of encephalitis or in a pure form. Examples of the former group are much the more frequent, those of the second group forming only 12 per cent. of the cases observed by the writers. The symptoms are relieved by rest and silence, and aggravated by sudden movements or noise. During the attacks of vertigo diplopia may occur. The condition is liable to be mistaken for neurasthenia, hysteria, gastric vertigo, cerebral arteriosclerosis and softening, Ménière's disease, disseminated sclerosis, and labyrinthitis due to other causes than epidemic encephalitis. The diagnosis is made by the presence of nystagmus, Romberg's sign, and the Babinski-Weil test. Treatment consists in the administration of quinine in doses of 10 or 5 cgm. two or three times a day, a considerable time after food. Several patients have derived much benefit from cachets containing stovain 0·01, pyramidon 0·20, and veronal 0·25.

Delater and Rouquier state that a form of epidemic encephalitis characterized by apparently *exclusively psychical symptoms* was described by them in 1920, and has since been observed by numerous writers, including Claude, Froment, and Comte, Abadie and Hesnard, and Guy Laroche and Filassier. Localizing signs in the central grey nuclei, pons, and medulla are either entirely absent or occupy a very subordinate position. Delirium, hallucinations, confusion, and mental disturbances of all kinds which used to be described under the name of acute delirium, dominate the scene, and the diagnosis can only be established by the subsequent development of acute transient and dissociated paralyses, myoclonus, or neuralgic symptoms. Delater and Rouquier report the first case on record in which the autopsy of such a case confirmed the diagnosis of epidemic encephalitis. No neurological symptoms were detected during life, and *post mortem* the lesions were confined to the cortex and meninges.

Chavigny and Gelma, of Strasbourg, illustrate the *medico-legal interest* of the psychopathic prodromes of epidemic encephalitis by relating the case of a man, aged 22, arrested for stealing a bicycle, who was found to be suffering from the disease.

Gosset and Gutmann record a case of lethargic encephalitis with *lumbo-sacral localization.* The patient was a man aged 41, who presented a marked febrile condition for 24 days, accompanied during the first half of this period by somnolence, and in the second half by polyuria of sudden onset and termination and by retention of urine, the last symptom being associated with loss of one ankle-jerk and diminution of the other for two months. Involvement of the central nervous system was shown by somnolence, followed by insomnia, myoclonus, and characteristic neuralgia. The writers conclude that in addition to the ordinary localization of the virus there was an involvement of the terminal segments of the lumbar cord and first sacral segments, in which the centre for the ankle-jerk and vesico-spinal centre are localized. The cause of the polyuria was probably involvement of the infundibular region.

Kennedy, of the Bellevue Hospital, New York, states that the *peripheral nerves and spinal roots* are affected in encephalitis to a considerable degree, and quotes Abrahamson to the effect that unmistakable signs of radiculitis were present in 60 per cent. of his cases. Palsies of single cranial nerves are not uncommon, the second and third being those most usually affected. Single peripheral nerve-trunks are also sometimes involved. The prognosis in the peripheral and radicular types is good, so that pathological confirmation of the clinical diagnosis by autopsy could not be obtained. Examples of undoubted polyneuritis on an encephalitic basis are less common, according to Kennedy, than the radicular types or those in which isolated nerve-trunks, such as the facial, are involved.

Müller, of the Marburg University Medical Policlinic, draws attention to the increased frequency of cases of so-called ‘rheumatic’ facial paralysis since the appearance of epidemic encephalitis, and maintains that they are really only abortive forms of an infective nervous disease, principally affecting the pons, just as similar cases may be caused by the virus of epidemic poliomyelitis.

Sainton and Cornet describe the following two *new signs* of epidemic encephalitis. The first sign consists in the possibility of provoking myoclonic movements by percussion of the upper limbs, masseter, or trunk muscles. The second sign is shown by a delay in the contraction of the frontalis muscle when the patient is made to look upwards. This sign, like disturbance of symmetrical movements of the eye-muscles characteristic of epidemic encephalitis, indicates an involvement of the mesencephalon.

Masci, of the Ospedale Policlinico Umberto 1 of Rome, draws attention to a remarkable phenomenon, observed in the parkinsonian state following lethargic encephalitis, which consists in the fact that patients who are barely able to walk have no difficulty in running. A study of the literature showed that this sign had already been described by Tilney, who had given it the name of ‘ metadromic progression ’, and by Souques, who called it ‘ paradoxical movement ’.

In a paper on *affection of the optic nerve* in epidemic encephalitis, Waardenburg, of Arnheim, states that it used to be taught that the motor apparatus of the eye was exclusively affected in this sense, while vision remained intact. Subsequent observations, however, showed that this view was incorrect, cases of optic neuritis and optic atrophy being reported by Economo and Bartels, Oberndorfer, Hiram Woods, and Schumway. Waardenburg himself has observed one case with a central scotoma indicating a retrobulbar neuritis, and another case with a slight peripheral limitation of the visual field.

In the Ministry of Health's report, Parsons states that of 234 cases in which the fundi were examined, optic neuritis was present in 5·5 per cent., and in 19 per cent. the several signs which were observed formed part of the ophthalmoscopic picture of optic neuritis.

Mongini, of Ferrara, reports a unique case of lethargic encephalitis of cerebello-bulbar type in a woman aged 32, which commenced with bilateral amaurosis due to optic neuritis of about 30 days' duration.

Lafon, of Perigueux, reports the case of a soldier who had an attack of lethargic encephalitis in March 1920, and twenty months later still presented *paralysis of accommodation*, paralysis of convergence, and myosis. Lafon remarks that most writers regard the ocular disturbances of lethargic encephalitis as transient, but the persistence of the symptoms in his patient shows that one must not be too optimistic.

Arlt, of the Breslau University Eye Clinic, records a case of ambulatory lethargic encephalitis with *hemianopsia* in a girl aged 20. Apart from headache for a fortnight and hemianopsia, the patient had no symptoms, and complete recovery took place. Only four other examples of this complication have been recorded in encephalitis, only one of which, reported by Bychowski, of Warsaw, recovered, while the other three, described by Buzzard and Greenfield, ended fatally. Arlt's is the only case in which hemianopsia was practically the only symptom and was of such a short duration.

At a meeting of the Académie de Médecine on July 25, 1922, Guillain, Kudelski, and Lieutaud recorded a case of lethargic encephalitis in a woman, aged 25, presenting *Mikulicz's syndrome* of enlargement of the lachrymal, parotid, and submaxillary glands. No previous example of this condition appears to have been described either during, or in convalescence from, lethargic encephalitis. In the subsequent discussion Netter stated that though he had never seen enlargement of the lachrymal glands in epidemic encephalitis, he had seven times observed swelling of the salivary glands. In three cases both the parotid and submaxillary glands were affected, in two the parotids only, in one the submaxillary glands only, and in one only the right parotid.

Marie, Binet, and Lévy have been impressed by the frequency of *respiratory disturbances* in epidemic encephalitis, especially in children, and attribute most, if not all, of these disturbances to organic lesions of the nerve centres. The symptoms consist of (i) respiratory disturbances properly so called, such as polypnoea or tachypnoea, which may be permanent or paroxysmal, bradypnoea and apnoea; (ii) spasmodic cough resembling pertussis but without expectoration or prolonged inspiration; (iii) respiratory tics, consisting in (*a*) blowing through the mouth and nose; (*b*) sniffing, almost always associated with frequent spitting and mental disturbances.

Vincent and Bernard have also observed a large number of cases of acute or chronic encephalitis accompanied by various respiratory disturbances, either alone or in association with those described by Marie and his pupils. In some of their cases the respiratory mechanism was affected, as was shown by deformity and immobility of the base of the thorax, and in others the respiratory disturbances consisted in acute pulmonary oedema.

Independently of these French observers, Adler remarks that respiratory symptoms usually consisting in transient attacks of dyspnoea are frequent in epidemic encephalitis. The patients are also apt to complain of shortness of breath, which accounts for their constantly keeping their mouth open, a symptom often seen in other diseases of the corpus striatum.

Barach and Woodwell, of Boston, report two cases of lethargic encephalitis in which the development of an extreme type of shallow breathing was attended by deep cyanosis and coma. The arterial blood was markedly deficient in oxygen, and contained an excess of carbon dioxide. Inhalations of oxygen greatly relieved the arterial anoxaemia, but had no effect on the steady accumulation of carbon dioxide. The circulation was much improved at first by the relief of the anoxaemia, but progressive cardiac failure developed later, probably owing to the retention of carbon dioxide. The writers think it probable that a terminal involvement of the respiratory centre is sometimes the cause of death in lethargic encephalitis.

Tracings showing disturbances of respiratory rhythm in ten cases of chronic encephalitis will be found in the article by Bilancioni, of the oto-rhino-laryngological clinic, and Fumarola, of the clinic of nervous and mental diseases, of the University of Rome. Laryngoscopic examination of these patients showed a certain degree of sluggishness in adduction and abduction of the vocal cords, and in rare instances an actual paresis and paralysis of one half of the glottis.

Owing to the close relation between *hepatic lesions* and disease of the corpus striatum as exemplified in Wilson's disease, Stern and Meyer-Bisch decided to study the disturbances of liver function in epidemic encephalitis. In ten cases examined in the chronic stage there was invariably urobilinuria, which sometimes reached an extraordinarily high degree. Occasionally reducing substances occurred spontaneously in the urine, but in such small amounts that a polarimetric investigation was impossible. Their presence was most marked after tests with laevulose. In all cases there was a disturbance of carbohydrate metabolism which was manifested by distinct hyperglycaemia or by prolonged excretion of reducing substances or both. These investigations thus showed that in the residual stages of epidemic encephalitis, especially in the chronic amyostatic form, there is a marked disturbance of the liver function.

Bénard alludes to the cases reported by Briand and Rouquier and Dopter (see *Medical Science*, 1921, **5**, 198) and records an example of extreme *polyuria* (20 litres in 24 hours) which was apparently due to two different causes, according to the stage of the disease at which it was observed. In the first stage, when the amount was 17–20 litres, it was decidedly influenced by injection of pituitary extract. On the other hand, psychotherapy during this period was ineffectual, and injection of anything but pituitary extract had no result. During the second stage, in which the polyuria did not exceed 10–13 litres, pituitary extract produced some effect, but a much less pronounced and immediate one, whereas psychotherapy was quite successful.

Stern, of the Göttingen University Neurological Clinic, remarks that *disturbances of the genital function* have often been observed in epidemic encephalitis, but almost always in the form of sexual enfeeblement. Exaggeration in the function of the genital system in this disease is very rare, the only case of the kind being that reported by Pilcz (see *Medical Science*, 1921, **5**, 199). Stern himself has also observed increase of sexual appetite and an impulse to masturbate in the group of amyostatic patients. He now describes a syndrome of which he has not found a single example in the literature, viz. precocious puberty following an attack of lethargic encephalitis in a boy aged 13, who had previously shown signs of infantilism. In the absence of an anatomical examination the cause of the condition could only be conjectural. There was no evidence of a testicular or suprarenal tumour, but Stern thinks that it was most probably due to involvement in the encephalitic process of the pineal gland, affection of which is often associated with precocious puberty.

Guillain and Gardin state that the recent literature shows that *pregnancy in epidemic encephalitis* is sometimes normal, or that encephalitis may be aggravated by pregnancy, or that premature delivery may occur after death of the foetus, and that sometimes abortion has had to be induced owing to the mother's life being in danger. The child may die *in utero* or be born in a normal condition, or show symptoms of encephalitis after birth. With the exception of those published by Valentin and David, and by Rathery and Cambassédès respectively, in which pregnancy developed in women who already presented the post-encephalitic parkinsonian syndrome, all the previous cases were examples of acute encephalitis occurring in pregnancy. Guillain and Gardin now report the case of a woman, aged 28, who became pregnant five months after the onset of lethargic encephalitis, when a parkinsonian syndrome was already well established. Pregnancy pursued a normal course and a healthy child was born at full term, though labour was unusually slow and required the application of forceps. After confinement no change occurred in the parkinsonian syndrome, but the woman's state remained the same as before.

Marinesco records two fatal cases in which lethargic encephalitis developed in the fifth and the seventh month of pregnancy respectively, with histological examination of the nervous system in one case.

In a series of 50 women, aged from 17 to 46, who were either pregnant at the time of their illness or developed encephalitis after confinement or within the period of normal lactation, Parsons states that the mortality was nearly 50 per cent., but after exclusion of 7 cases in which pregnancy was a more or less remote antecedent, this figure became reduced to 44 per cent., which represented the general mortality of women between 20 and 40 who contracted lethargic encephalitis during 1919 and 1920.

At a meeting of the Académie de Médecine on May 31, 1921, Mercier, Andrieux, and Bonnaud, of Tours, reported the case of a primipara who on the twenty-second day of an attack of encephalitis with a myoclonic onset gave birth to a living child and died on the fortieth day. The child had a slight attack of encephalitis, which was manifested by myoclonic convulsions in the second week, but recovered. The case is of interest as showing that epidemic encephalitis which had started three weeks before term and had not been treated did nevertheless not cause premature delivery or the death of the child. Confinement appears to have acted as a traumatic shock and to have aggravated the mother's condition. In the subsequent discussion, Achard (2) related a case showing that though placental transmission of lethargic encephalitis is possible it does not invariably occur.

His patient was a woman aged 25, who gave birth to a six months' foetus a few hours before death, after an illness of twelve days. Histological examination of the mother's brain showed typical lesions of lethargic encephalitis, whereas the brain of the foetus was normal.

Parsons states that some form of *eruption* was described in 92 of the 1,250 cases of lethargic encephalitis reported to the Ministry of Health. Erythema, which was noted in 16 cases, was the most frequent variety. In certain cases the eruption simulated the rash of scarlet fever, measles, or typhoid fever. Herpes labialis was noted in 11 only, herpes frontalis in 1, and herpes costalis in 1. As a rule the rashes were mild and evanescent, and no special symptoms characterized a case in which a rash appeared.

Netter has collected 5 cases of zosteriform eruption in epidemic encephalitis, 3 of which had been already recorded and 2 had been under his own care. The distribution was intercostal in 3, ophthalmic in 1, gluteal in 1. In 4 cases the eruption was undoubtedly due to changes in the intervertebral ganglia, like those described in vertebral trauma, Pott's disease, cancer of the vertebrae, ataxia, &c., and should be described as 'zosterian' rather than as 'zoster'. The last term was applicable only to the fifth case, in which the eruption developed after exposure to varicella.

Price, of Spokane, Washington, reports a fatal case, in a girl aged 7 years, of *recurrence of symptoms* 18 months after apparent recovery, death being due to respiratory paralysis. He points out that in encephalitis as in poliomyelitis evidence is accumulating that an actual second attack with reinfection from an external source probably occurs in rare instances. The possibility of a relapse in epidemic encephalitis after a year or longer is of interest to life insurance statisticians, who are already somewhat chary of renewing health policies to persons who have had lethargic encephalitis.

Apert and Vallery-Radot, of Paris, record the case of a child, aged 14, who three months after an attack of lethargic encephalitis developed right facio-palpebral spasm with a slight disturbance of gait resembling that which occurred during the first attack. Complete recovery took place. The writers allude to another case in which there was not an entire recovery between the two attacks, but merely a remission and complete apyrexia.

Parsons states that relapses were said to have occurred in about 20 cases only of the 1,250 included in the Ministry of Health's report. In a certain proportion of these, however, the term 'relapse' was probably incorrect. In two cases reinfection could not be excluded; in another instance the patient did not relapse into a former condition, but developed manifestations of the disease after an interval of some weeks or months.

In his description of the *sequelae* of the epidemic of 1919–20 Beriel, of Lyons, gives the name of 'Wilsonian forms' to a series of cases in which the symptoms resemble those of Wilson's disease. He describes the following 3 varieties: (1) Typical Wilson's disease, characterized by predominance of rigidity in the upper part of the body with spasms and eccentric attitudes of the head, mouth, and tongue, and tremors resembling those of paralysis agitans. (2) Pseudo-sclerosis type, characterized by a lesser degree and extent of spasticity, intention tremor, nystagmus, and exaggeration of reflexes, resembling disseminated sclerosis but without characteristic lesions. (3) Torsion spasm, characterized by predominance of tonic spasms of the limbs, neck, and trunk, hypotonus of certain muscular groups being associated with hypertonus. Other cases of torsion-spasm following lethargic encephalitis are reported by Mourgue, of Bordeaux, and by Vignard, Mouriquand, and Léorat, of Lyons.

House, of Portland, Oregon, classifies the sequelae in his cases of epidemic encephalitis into the following four groups: (1) Myoclonic movements which had persisted from the acute stage, though with steadily decreasing severity. This was the least numerous group. (2) Definite psychoses, the commonest of which was dementia praecox. (3) Neurasthenia or psychasthenia, or both. This was the largest group. (4) Gross organic lesions of the brain or cord, viz. (*a*) unilateral brain lesions producing hemiparesis, (*b*) lesions limited to the pons or medulla, or both, causing persistent oculomotor or bulbar disturbances, (*c*) disseminated lesions shown by parkinsonian symptoms.

Paterson and Spence investigated the after-affects of epidemic encephalitis in 25 cases aged between 3 months and 11 years observed by them in the Hospital for Sick Children, Great Ormond Street, or in the children's ward at St. Thomas's Hospital, London. Although only one case was fatal, only one-fourth made a complete recovery. The mental changes varied from complete idiocy to slight mental deficiency and also showed themselves as affections of the character and habits of the child. The physical changes included spastic diplegia, hemiplegia, symptomatic paralysis agitans, muscular rigidity, and tremors. The younger the child at the onset of the disease and the longer the acute state of the illness, the greater was the degree of subsequent mental deficiency.

Boyd, whose paper on an outbreak of lethargic encephalitis at Winnipeg was noticed in a previous review (see *Medical Science*, 1920, **2**, 406), found that complete and rapid recovery was uncommon except in really mild cases, that many patients continued to suffer from some of the symptoms in a modified form, and in a few nervous symptoms appeared which must be regarded as true after-affects. Of 31 patients communicated with, whose attack had occurred in the October 1919–January 1920 epidemic, 20 complained of symptoms after all the acute manifestations had disappeared, these symptoms being either general, paretic, irritative, or parkinsonian. In several cases in which facial paralysis was a feature of the acute stage a lingering weakness was detected many months later, but in no case was the paralysis complete or even pronounced. Diplopia was a more common symptom. In some it was a feature from the beginning of the illness; in others it came on after an interval of apparent recovery. Weakness of accommodation was perhaps the most frequent indication of cranial nerve weakness.

According to Hofstadt, of the Munich University Children's Clinic, the most frequent and earliest sequel of epidemic encephalitis is the peculiar disturbance of sleep (see *Medical Science*, 1921, **5**, 198–9) which is so constant that its occurrence justifies a retrospective diagnosis of encephalitis. Hofstadt goes so far as to assert that a disease supposed to be lethargic encephalitis can only be regarded as such when this symptom occurs. The insomnia was found not only in cases which had otherwise completely recovered, but as a prodrome or accompaniment of the amyostatic or choreo-athetotic complex, and almost always in cases in which psychoses developed.

Thomas, of the Cologne University Children's Clinic, records two cases in children aged 5 and 12 years respectively, in whom rhythmical twitchings in sleep occurred as a sequel, the left sterno-mastoid in one and the left corner of the mouth in the other being affected. In both cases the twitchings were present at the end of the febrile period, and in one case they were présent during the day as well after termination of the acute stage. In one case the movements were exaggerated during sleep. Their occurrence is attributed to the persistence of an inflammatory focus.

Pette, of the Hamburg University Neurological Clinic, records six cases with well-marked parkinsonian symptoms which did not develop until a considerable time after the acute stage. It was a remarkable fact that the primary disease had not been severe in any case, and in one had been so mild that work had not been interrupted. All the patients had been fit for work at first after recovery from the acute stage, but were not so any longer. Pette asserts that no cases have hitherto been recorded in which there has been so long an interval as 15 months, which occurred in one of his cases, between the acute attack and the sequelae.

Prognosis. Sanz (2), of Madrid, states that the mortality of epidemic encephalitis varies with the time and place at which the disease has been studied. According to Banús it ranges from 25 to 31 per cent.; in Spain, however, it has been much less, approximately 10 per cent. Chalier estimated it as high as 40 or even 50 per cent. and attached an unfavourable significance to the progressive evolution of myoclonic movements. The mortality in Sanz's cases was 17·64 per cent. All these figures refer to the acute stage of the disease. In the chronic stage the danger to life is less, but the prognosis is unfavourable owing to the persistence of symptoms which interfere with the patient's power of locomotion. Moreover, there is always the possibility of a reappearance of the principal symptoms, though this is a fairly uncommon event. The motor sequelae tend to subside slowly with alternate recrudescences and remissions, but in some cases persist indefinitely and defy all methods of treatment. In addition to parkinsonism, which is the most frequent sequela of epidemic encephalitis and one of the most refractory to treatment, Sanz mentions a cerebellar form of disseminated sclerosis and a chronic serous meningitis as sequelae. Lastly, as an aggravating factor in the prognosis of epidemic encephalitis, should be mentioned the state of depression into which the patients fall owing to the apparent incurability of their condition, with the result that some show a dangerous tendency to suicide.

In a paper based on the study of 97 cases of epidemic encephalitis from which early fatal cases were excluded, Bing and Staehelin, of Basle, come to the following conclusions: (1) Pure epidemic hiccough clears up entirely without any residues. (2) Other rudimentary forms in which lethargy, chorea, and myoclonus are absent are not so completely harmless as pure hiccough, but appear to end in complete recovery also. (3) Lethargic forms with or without symptoms of myoclonus or chorea clear up entirely in about 25 per cent. In almost half the cases parkinsonism supervenes sooner or later. In a minority of the cases it occurs as a later sequel, usually after about six to nine months' apparent recovery, but sometimes not till the end of a year. (4) Pure choreic forms have a relatively favourable prognosis, as the writers have never seen parkinsonism develop in such cases. (5) The myoclonic forms are more serious than the choreic, as pure myoclonic encephalitis may be transformed into parkinsonism. (6) Post-encephalitic parkinsonism may clear up, but this is exceptional, and apparently only occurs in cases in which the parkinsonism is not of late onset. (7) The mortality of epidemic encephalitis, after exclusion of pure hiccough and other rudimentary forms is about 20 per cent. Death in late cases may be due to febrile complications or suicide and also to the direct consequences of parkinsonism.

Adler, of the First Medical Clinic of the German University at Prague, states that, up to March 1922, 77 cases of epidemic encephalitis, of which 35 were males and 42 females, were admitted to the clinic. With the exception of three cases which occurred in the early months of 1922, all belonged to the 1920 epidemic. Only 9 or 12·9 per cent. completely recovered, 7 died in the acute or subacute stage, and 6 in the chronic stage, including one death from intercurrent typhoid fever and another from intestinal obstruction. The mortality was therefore 16·9 per cent. Of the remainder only 6 or 7·9 per cent. were partially capable of work, while the rest, consisting of 48 cases or 62·3 per cent., were more or less completely unfit. Of the 20 acute cases 5 died, 4 made a complete recovery. and the remaining 55 per cent. drifted into the chronic stage. The cases which completely recovered belonged to the lethargic or choreiform type of encephalitis. Adler points out that the severity of the acute stage is no guide as to its subsequent course. None of the 51 patients who developed the parkinsonian syndrome recovered.

Hall, of Sheffield, who records his observations in 30 cases, states that patients with comparatively mild attacks recover only to be seriously damaged for very long periods, even permanently. Others who appeared in the early stage to be at death's door recovered quickly and completely, while still others, who seemed to have moderately severe attacks for one or two weeks, suddenly became worse and died without obvious reason.

Parsons states that of the 1,273 cases notified from England and Wales during 1919 and 1920 the case mortality was 48·3 per cent. The death-rate in young children was particularly high, being 75 per cent. in the first year and 67·5 per cent. in the quinquennium 1–5. With each succeeding age period the percentage figures decreased until the quinquennium 10–15 when the mortality was 33·1 per cent. From this point the mortality steadily rose without any break until it reached 80 per cent. in the age period 70–80.

Treatment. Among the numerous drugs recommended in the treatment of lethargic encephalitis, including salvarsan, electrargol, eucupin, &c., Economo has found only two which have a really favourable influence upon the disease, viz. urotropine and Pregl's iodine solution. Urotropine should be given in large doses of 4–8 gm. at a time intravenously for four or five injections and then internally. Pregl's iodine solution should be given intravenously in doses of 10 c.cm. the first day, 25 c.cm. the second day, 50 c.cm. the third day, 100 c.cm. the fifth day, and then 100 c.cm. two or three times a week till a total amount of 800 c.cm. has been given.

André-Thomas and Rendu report a case in which intravenous injection continued with internal administration of urotropine had a remarkably successful result, whereas Hume, Nattrass, and Shaw, who employed this method, found that it did not alleviate the disease in any way, although it was apparently innocuous.

Lust, of the Karlsruhe Children's Hospital, has found that the chronic insomnia following epidemic encephalitis described by Hofstadt and others (see *Medical Science,* 1921, **5**, 198–9), which is so refractory to ordinary hypnotics, is best treated by intramuscular injections of milk, in doses of 2 c.cm., the action of which is apparently connected with a rise in the body temperature, as the narcotic or sedative influence of this treatment was noted only as long as the temperature was raised. The injection of milk does not possess a specific influence, as other substances which cause a rise of temperature, such as sodium chloride, by mouth or subcutaneously, and to a certain extent hot baths and hot packs, have a similar effect. Lust suggests that the hypothetical sleep centre is in close proximity to the heat centre.

Piticariu, of Cernauti in Roumania, treated three cases of myoclonic encephalitis and one of parkinsonism by intravenous injection of the patients' own cerebrospinal fluid, the injections being given in doses of 10 c.cm. every 5–7 days. Shortly after the first injection a considerable improvement was observed, and the symptoms completely or almost completely disappeared.

Adler speaks highly of scopolamine in the symptomatic treatment of parkinsonism, and states that doses of from 1–5 mgm. may be injected without unpleasant after-effects. The drug is of chief benefit in mild cases, which are remarkably improved, if only for a short time, recurrence of the symptoms taking place when the treatment is suspended.

In a paper on the management of children presenting the post-epidemic encephalitis syndrome, Leahy and Sands, of New York, state that, from the study of the conditions of excitement seen in general paralysis and exhaustive states, they have come to the conclusion that the drugs usually employed as sedatives do more harm than good. In cases where a sedative must be employed, they have used paraldehyde, as that is the only drug with no cumulative action and is therefore the least harmful of sedatives.

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BOTULISM.

The rapid evolution of experimental medicine with the attendant shifting of the trend of thought from one level to another, such as from a purely clinical to a specifically aetiological, or from a purely biological to a physico-chemical, blurs in the train of its brilliant progress many clear lines of demarcation. Definitions are made according to the importance attached to certain of the many and constantly multiplying factors of a problem and not according to the complex as a whole. There is also an inducement to a critical attitude of mind, and not only are doubts expressed concerning widely held beliefs but the actual existence of experimental facts is sometimes challenged. In the purely laboratory domain, for example, the biological basis of the Wassermann reaction is supplanted by a physico-chemical hypothesis with the consequence that in this transitional stage it is being sometimes looked at askance. In the field of epidemiology one had recently to defend the microbic origin of Mediterranean dysentery against a challenge to its specific aetiology. Such conflicts might arise every day: thus, for example, what should be the definition of polio-encephalomyelitis? Is it solely an infection by the undefined virus of poliomyelitis or is it a 'clinical and epidemiological concept', various organisms being associated with its aetiology?

Infectious diseases one is accustomed to define easily since the manifold clinical manifestations may all be brought into causative relationship with the invading agent. But when this agent is obviously demonstrable, when it acts through the intermediary of its products and—paradoxical as it may seem—when the disturbed functions go to form a 'typical picture',—then the concept of the disease vacillates between that of a specific infection or intoxication produced by the virus and that of the 'typical clinical picture' without reference to the discovery of the specific agent. To be more concise, diphtheria is defined as a specific invasion by *B. diphtheriae*, but general paralysis of the insane—until recently—would be defined as a comprehensible complex of nervous and mental symptoms, but not as a specific infection by *Spironema pallidum* with a definite localization. This habit is not unattended by practical consequences when the necessity arises of determining the nature of diseases of a more or less unusual incidence.

Thus it is not surprising that the term 'botulism' has been applied to numerous cases exhibiting miscellaneous encephalic symptoms simply in the search for a similarity of the 'clinical picture', without any regard either to the history or the specific aetiology of the cases. Known since 1817 [1] as the 'true sausage poisoning', *botulism* must have comprised in the early writings of the first half of the nineteenth century, both outbreaks of food poisoning caused by agents other than its modern specific anaerobe and sporadic cases of, as well as 'family groups' of, more or less obscure infectious diseases with a peculiar localization in the encephalon. For, first, paratyphoid bacilli (Gärtner type) may occasionally give rise to food poisoning with nervous symptoms, and, secondly, different bacteria as, for example, the somewhat indeterminate *B. proteus*, may attack the central nervous system, while the habitat of *proteus* allows us to assume the possibility of its contaminating the most varied articles of food. On the other hand, in the absence of the objective evidence of an authentic examination of the incriminated meal, the connexion between its consumption and the supervening disturbance of functions must rest on the diagnostic faculties of the victim rather than on the unprejudiced opinion of the physician. When one reads contemporaneous descriptions of alleged individual cases of botulism, conceived as a specific intoxication by the bacillus, in which the only evidence adduced is that the patient had partaken of a food of everyday use which has been shown to be a good medium for the growth of the bacillus, one may acquit the writers of a hundred years ago for including in their essays every case of ophthalmoplegia in the category of sausage poisoning. They had no choice but to be guided by the clinical picture. Even to-day this picture is said to be so peculiar that the ordinary clinical observation is regarded as sufficient for the recognition of the disease. The definition of this condition in van Ermengem's words is simple (1): 'the picture is mainly made up of neuroparalytic disturbances of central origin. These processes find their expression in certain changes in the secretory functions of the digestive tract and in symmetric, generalized or localized motor paralyses caused by lesions seated in the ganglion cells of the bulbar and spinal nuclei'. A study of all the available literature has led careful American observers thus to describe the precise features of this picture:—

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[1] J. Kerner, the Swabian physician and poet, was the first to recognize and to describe the symptoms of genuine sausage poisoning in 1817. N. Paulus published in 1834 a more detailed account of sausage poisoning describing the ophthalmoplegic symptoms.

> 'The most striking effect on the nervous system is the difficulty in vision with normal background, dilated pupils, ptosis, paralysis of the various eye muscles and double vision, and disturbances in deglutition. Dizziness, sleeplessness, marked muscular weakness with no disturbance of the sensorium, no headache, and no anaesthesia or paraesthesia are characteristic. At times various paralyses of the different skeletal muscles, particularly about the neck, are seen. Practically all the cranial nerves, except the 1st and 2nd, have shown involvement . . . ; that is—
>
> Ptosis, mydriasis, disturbances of accommodation—3rd and 4th; inability to cry—lachrymal nerve of the fifth; dryness in mouth—7th and 9th; disturbances of deglutition partially due to lessened secretion and partially to nervous disturbances leading to difficulty in chewing and the muscular side of swallowing—9th, 10th, and 11th; mask-like expression—7th; at times difficulty in hearing—8th; variation in speech to aphonia—12th; constipation and respiratory and cardiac disturbances—10th.
>
> Further, the retention of the urine and the occasional paralyses of muscles of the limbs indicate that the spinal cord may be damaged at times. . . .
>
> The deep reflexes are not disturbed. Romberg and Babinski both absent. No tremor and no spastic conditions have been described. No angioneuroses of the skin were noted . . . The sensations of the mucous

membranes of the throat and mouth are dulled, probably because of its dry condition . . .'

Usually the neuroparalytic disturbances develop progressively; the onset is marked by amaurosis caused by a more or less complete paresis of accommodation, and accompanied by ptosis, diplopia, &c. The ophthalmic symptoms are very persistent, they may be present for weeks or months *without the slightest lesion of the disk being detectable*. In the end there is a complete restitution. The symptoms develop usually 12 to 24 hours, sometimes 36 to 48, after the consumption of the toxic food. Relatively often there is a prodromal period of general ill feeling, vomiting, and diarrhoea, but these manifestations disappear within 2 to 3 days.

The secretory disturbances are very marked; there may be either a complete dryness of the pharyngeal mucous membranes with the affection of vocal cords (these may be paralyzed and anaemic decubital ulcerations formed) or a hypersecretion leading to an agglomeration of sticky mucus filling up the air passages and provoking a characteristic feeling 'as if there was a shelf in the throat beyond which food could not pass, but which did not hurt'. In effect—a membranaceous angina may be simulated and croupy cough is not infrequent. The inability to swallow liquids and their return through the nose are particularly noted. A very common symptom is the paralysis of the stomach with the consequent retention of the food for some days. In certain cases the evacuated gastric contents proved to be toxic for animals. In the later stages the bulbar manifestations are very pronounced, such as rapid, superficial respiration; attacks of dyspnoea; slow pulse. No coma; patients lie motionless, but will answer sensibly all questions and do not lose consciousness even before death. *There is no fever* unless of a secondary nature, as, for example, when painful parotitis supervenes.

The mortality in severe cases reaches 30 to 50 per cent. Death usually occurs suddenly in the first or second week, and is due to a paralysis of the diaphragm, the heart beating for some 20 min. after death. It takes place later but seldom, and then sometimes with the histological post-mortem picture suggested to be that of polio-encephalo-myelitis.

Such is the classical clinical picture, and it may be readily admitted that certain peculiarities, as the invariably normal condition of the disk or the absence of fever, tend to make of it a 'nosological entity'. But the differential diagnosis covers a larger field of possibilities, and poisoning with certain plant alkaloids, particularly belladonna, on the one hand, and the aetiologically obscure asthenic bulbar paralysis on the other, present real difficulties in differentiation. In fact, the most certain means of diagnosis is the evidence of food poisoning in individual cases or that of commensalism in an 'outbreak'. For the clinical picture would be incomplete without the mention of abortive cases, and these are the most difficult to class. A whole scale of gradations has been recorded: some cases present transient disturbances of vision or of swallowing, others a general 'malaise' with gastro-intestinal disorder, others again various degrees of muscular paresis evidenced in feeling, for example, 'that tongue seemed hard to move', or 'jaws seemed very tired', or 'throat was filled up with mucus all the time', or 'legs and arms were almost powerless', or a passing diplopia and nystagmus were complained of.

These abortive cases would obviously escape recognition without evidence of commensalism. Similarly the classical cases would obviously fall into the category of a polioencephalic process without the evidence of food poisoning.

But even in its proper sense '*botulism*' is a misnomer, since it was the lumps of unminced ham which usually formed the contaminated ingredient in the sausages, and it was in fact smoked ham which was the toxic article in the majority of authentic cases. Game and poultry, as well as fish, both canned, smoked and salted, have been found to be responsible for botulinus poisoning. Molluscs, crustacea, canned vegetables and fruit (and cheese) have also been responsible for outbreaks of botulism, particularly during recent years.

It was not until 1895 that an end was put to various speculations as to the nature of the toxigenic agents causing botulism by the discovery of *B. botulinus* by van Ermengem at Ellezelles in Belgium in an outbreak extending to some 30 cases with 3 deaths. The bacillus was shown to be an obligatory anaerobe. It was found in the intermuscular connective tissue of the toxic ham, which bore no signs of alteration, save for a rancid smell, and tasted wholesome. The bacillus was also recovered from the spleen and the large intestine of one of the fatal cases. The ham proved toxic by subcutaneous injection to cats, pigeons, monkeys, rabbits, guinea-pigs, and mice, the last four species being equally susceptible to its ingestion. The animals exhibited miscellaneous symptoms characteristic of botulism, and it was thus proved that the bacilli possessed the peculiar neurotoxic affinities. The anaerobic bacilli were not, however, recovered from any of the animals, and van Ermengem concluded that it is the toxin produced by the bacilli in the ham, and not their growth in the body which cause the symptoms of botulism.

Thus a definite outbreak of botulism was identified with a specific organism, and it was shown that one group of food poisoning is caused by a toxigenic bacillus attacking the central nervous system.

Five years later, in 1900, Römer investigated in Gaffky's Institute a ham, the consumption of which caused ophthalmoplegic symptoms in 4 persons in a small village in Germany (the district of Alsfeld). Some portions of the ham which smelled rancid appeared altered, and their cultivation yielded a growth of an anaerobic bacillus similar to that found at Ellezelles.

Four years later, in 1904, Gaffky and Landmann investigated an outbreak in which 21 persons were taken ill at Darmstadt after the consumption of tinned beans. Of the 21 persons affected 11 died within 4 or 5 days, all cases exhibiting classical symptoms of botulism save for the fact that there was but slight mydriasis.

The remainder of the toxic tin, which also exhibited a rancid smell, grew an anaerobic organism which very closely resembled the Ellezelles bacillus without being rigorously identical with it.

In 1901 Madsen investigated a salted mackerel which had caused ophthalmoplegic disturbances and other characteristic symptoms of botulism in three persons of a family at Orö, in Denmark, one of the cases dying within 24 hours. He found that the fish, which exhibited the rancid smell, was contaminated by an anaerobic organism in small numbers. The brine in which the fish was kept yielded on filtration through porcelain a toxin which was neutralized by an antitoxic serum prepared in the meantime against the bacillus of Ellezelles.

In 1906 van Ermengem examined a ham, the consumption of which caused in 8 persons of a Flemish family of twelve (at Iseghem), typical ophthalmoplegic and other symptoms which disappeared in a few weeks, the cases recovering completely. He grew an anaerobic bacillus closely related to his original Ellezelles strain, but differing in some cultural characteristics as well as in so far as it produced a very much less active toxin.

Bürger investigated two family outbreaks of typical botulism in Berlin caused by the consumption of a ham prepared at a Pomeranian farm from a healthy home-killed animal, and brought as a present by the farmer's wife to the two related families. In the first family of four all members fell ill, and two daughters aged 14 and 2½ died after a week. Bürger recovered a typical *B. botulinus* from the spleen of the younger child.

In the second family of four, three members were affected, one of them dying after 14 days, but no anaerobic bacteria were obtained on post-mortem examination.

The toxic ham, which showed no macroscopic changes, and exhibited the familiar rancid smell, was examined also by Lentz at the Institute of Infectious Diseases in Berlin. He isolated from the rancid fatty portion an anaerobic organism which was minutely investigated by Ornstein and proved to be identical with the Ellezelles strain.

Schumacher enquired into a family outbreak in Rodt, Trier-Land Germany. Of the 10 members of the family 3 adults and 3 children had partaken of a raw ham and developed typical symptoms of botulism, two of the adults dying. Of the four other children who remained healthy none ate the raw ham, and one partook of it after it had been boiled. No bacteria were recovered from the organs, but the ham yielded on cultivation a typical *B. botulinus.* The ham proved toxic to mice on ingestion. A dog belonging to the family helped himself to the ham and survived, although it was not well for some days.

In 1913 Bürger investigated another family group of four in Berlin who all fell ill after partaking of a 'blood sausage'. Two women had but slight gastro-intestinal symptoms for a few days, while two men developed a typical picture and suddenly died after six days. From the spleen an anaerobic growth was obtained which corresponded with that of *B. botulinus,* but no pure cultures were isolated and thus the strain remained unidentified. The sausage was examined with a negative result.

In 1917 Dickson published a record of his investigations into the prevalence of botulism in California and on the Northern Pacific Coast, (along with some experimental studies on various strains of *B. botulinus*) and stated that in three out of eleven outbreaks of botulism observed during the previous six years he had succeeded in isolating *B. botulinus* from portions of discarded food.

Schürmann in his analysis of the work of the public health laboratory of the Hygienic Institute at Halle for the year 1915 mentions the fact that '34 times meat or sausages were sent for the discovery of the food poisoning bacteria. The presence of *B. botulinus* has been successfully proved twice in the case of the sausages'.

So far as can be ascertained these are the authentic occasions on which *B. botulinus* was isolated either from cases of botulism or from 'botuligenic' food. It will also be noted that not all of the thirteen 'botuligenic' viruses were in all respects identical. Four were shown conclusively to correspond exactly with the characters of the original virus (Ellezelles, Alsfeld, Orö, Berlin-Ornstein). One, the Darmstadt virus, is admittedly a definite variant of the type. Another, the Iseghem strain, is regarded by van Ermengem himself as an aberrant member of the family. The Treves virus does seem to behave morphologically, biologically and pathogenically like the Ellezelles strain but the final serological proof is lacking. As to the Berlin-Bürger and the U.S.-Dickson strains it is not possible to form a judgement because their characters are not fully described. The Schürmann strains isolated as they were at Römer's Institute may be presumed for this reason to be genuine but there is no evidence as to their precise identification.

Before entering on the discussion of the significance of these bacteriological findings it must be emphasized that the related eleven instances do not exhaust by any means the list of groups of undoubted food poisoning giving the picture of botulism without, however, *B. botulinus* being discovered. On the contrary, the medical literature of the last few years contains an ever increasing record of such cases.

Thus Schede carefully describes the history of a family of five who were all poisoned by the commensal consumption of a raw ham and developed all the classical symptoms. Umber, in whose clinic the patients were treated, refers to another case which he saw in 1915 at Stettin.

Dorendorf describes in detail five cases amongst German soldiers, all admitted to a War hospital in September, 1916. Two, one of which was fatal, were classical examples of botulism following directly on a meal of tinned liver sausage which formed part of the regular issue. For the other two cases this connexion was highly probable though not quite definite, while the fifth was taken ill in the trenches with violent gastro-intestinal disturbances, developed quickly 'typical symptoms' and was sent to hospital for 'deafness' and here his condition was diagnosed as 'botulism'. It is worth noting that the injection of the antitoxic serum prepared by Ornstein had immediate effects, though it did not save the life of one patient.

Nonnenbruch reports a successful cure of a case of typical botulism in a soldier by means of three intramuscular injections of the Ornstein antitoxic serum.

Paulus records a fatal case, one of a group of four who had all typical symptoms following the consumption of an 'under-smoked' and 'under-salted' ham and sausages.

During recent years, however, America has furnished most of the cases of 'botulism'. A leading article in the *Journal of the American Medical Association* draws attention to a great increase in the incidence of cases of food poisoning, due, in the writer's belief, to the fact 'that meats and vegetables prepared in the home are more likely to give rise to botulism than those prepared in large canning factories in which steam under pressure is used'.

Reference is made to Jordan who learned through 'press clippings', &c., that from October, 1913 to October, 1915, there were recorded 657 group and family outbreaks and 357 individual cases involving in all some 5,000 persons. The article does not assume *all* these cases to have been botulism and recommends that food poisoning be made notifiable in order that proper enquiry should allow of a correct differentiation being made.

That all the alleged cases are not 'botulism' is indeed only too apparent from reference to the American literature.

Thus, Lancaster reports (twice) as 'a case of botulism' a case of acute paralysis of the muscles of the eyes, throat and various other parts of the body with very rapid onset, absence of sensory and gastro-intestinal symptoms, and a condition of somnolence as the striking features. There was a very slow recovery. No reliable food history was obtained, and the case was frankly diagnosed as 'botulism' by exclusion. It may be pointed out, however, that there was no disturbance of the secretory functions so characteristic of the classical picture, and on the other hand persisting vomiting and tremor of hands were symptoms very unusual for 'botulism'.

Recent reports in the public press and in medical literature in the United States of America which suggest that many cases of encephalitis lethargica are in reality cases of botulism are discredited. One case has been described which closely resembled encephalitis lethargica and which proved to be botulism, the B type of *B. botulinus* being recovered from the medulla.

Again, Bine relates the history of two fatal cases whose illness, and death, is ascribed to the drinking of 'clam juice'. The symptoms certainly indicated an acute poliencephalic condition; there was a 'cataleptic' state of the muscles of the head, not characteristic of classical 'botulism'; no disturbances of the secretory functions were noted, the disk was not examined, all the extremities were paretic; no other persons were known to have been affected by the 'clam juice' in question and no bacteria were isolated from it. There is not even corroborative evidence of a post-mortem examination.

In short these are examples of obscure cases with polioencephalic symptoms without evidence of either 'botulism' or of specific intoxication by the B. botulinus.

There are on record, however, numerous instances of genuine botulism in the United States. Characteristically enough, the American outbreaks were as a rule connected with canned fruits and vegetables, whereas, as has been shown, the European cases were mainly due to meat or fish[1]. Dickson analysed eighteen American outbreaks with a known source of origin and found that eleven were due to food of vegetable origin as against seven of animal origin[2]. For some of these outbreaks the evidence of botulism is but presumptive. Thus Peck, quoted by Dickson (1915), reported in 1910, 'a series of eleven fatal cases of "ptomaine poisoning" in which death followed the eating of "sour" home canned pears and in which the symptoms he described were very similar to those observed in botulism'. Also, 'quite recently there was an epidemic in Fallbrook (Dickson (1915)) in Southern California in which a diagnosis of botulism was made and in which the most probable cause of the poisoning was spoiled home canned apricots'.

There are, on the other hand, reports of outbreaks of classical botulism. Thus P. Stiles, a lecturer in physiology, describes in an exquisite style, the symptoms which he himself developed after the consumption of minced chicken, the incriminated 'botuligenic' ingredient being the liver portion. Wilbur and Ophüls give a detailed account of a typical commensal outbreak at a student's club of the Stanford University in November, 1913. Twenty-four young people had a meal consisting of roast beef, string bean salad with mayonnaise dressing, gelatine pudding and whipped cream. Some had also mushrooms. String beans was the only common food for all the twenty-four, of whom twelve were taken ill. The symptomatology of the cases was described on the preceding pages of this article. Two kinds of string beans were consumed, one prepared at a factory and another, a light green variety, made at the home of one of the girl students. It was boiled for one hour on three successive days. This was the one partaken of by the whole group; all the cases incubated for 36–48 hours—one died on 13th day from sudden paralysis of the diaphragm.

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[1] The foodstuffs, &c., accepted as 'botuligenic' by van Ermengem (l.c.) on the basis of his analyses of the literature until 1912, were the following: sausages, ham, tinned meat, venison and poultry paste, stuffed geese, meat patties, pickled or smoked herrings, salted mackerel, salmon, sterlet, sturgeon, cray-fish, oysters, and beans.

[2] One instance each of spoiled beef, minced chicken, canned pork and beans, tamales (?), sausage, &c., bottled clam broth. The vegetable origin was as follows: home canned pears, apricots, corn, asparagus, commercially canned beans or spinach—one each, and home canned string beans—six times.

B. botulinus was not found, but the examination of the incriminated cans revealed the presence of a 'bacillus Turné', dreaded by fruit, &c., canners on account of its heat resistant spores 'which are able to spoil a whole batch when mixed with the raw product'. The following interesting analysis of several cases in an outbreak of botulism is characteristic in most respects.

Onset. Difficulty of vision was the first symptom in five cases, and vomiting in two. Abdominal pain was present with the vomiting in one case, and weakness was an accompanying symptom in two cases, in one of which it was very severe. The symptoms began within twelve hours in one case, twenty-four hours in one case, sixty hours in one case, and seventy hours in four cases. The onset was gradual, and in only one case was it of such a character as to cause apprehension of illness on the part of the patient.

Course. Once established, the disease became steadily and progressively worse in the fatal cases, excepting the one in which the patient showed some temporary relief for a few hours at a time. Death occurred in twelve hours in two cases, thirty-six hours in one, and seventy-two hours in two.

Gastro-intestinal symptoms. These consisted of vomiting and moderate general abdominal pain. They dominated the clinical picture in Case 6, and masked the neurologic syndrome in Cases 1 and 5. They were absent or negligible in the remaining four cases. It was observed that death occurred much more quickly in the patients showing gastric symptoms, and that so far as could be determined they ate more of the poisoned food than did the patients showing only nervous symptoms.

Nerve symptoms. With the exception of paralysis of the diaphragm, the motor lesions were confined to the cranial nerves. The olfactory (first), the trigeminal (fifth), and the auditory (eighth) nerves were not affected in any of the cases. The oculomotor (third), the trochlear (fourth), and the abducens (sixth) nerves were involved very early in every case. There was ptosis of one or both eyelids, and diplopia and paralysis of one of the ocular muscles, in two of the cases the right external rectus being affected. In only one of the cases was mydriasis present, Case 2. Nystagmus was observed in Case 6. Vertigo was not seriously complained of by any of the patients. The facial (seventh) nerve showed involvement in Case 2, in which paresis of the face appeared. The paralysis involving the glosso-pharyngeal (ninth) and the vagus (tenth) nerves were the most distressing features of the illness and occurred in every case. The difficulty of swallowing appeared shortly after the disturbances of vision, and sooner or later complete paralysis ensued. Suffocation generally followed attempts to swallow. Though there was no excess of secretion, there was an annoying accumulation of mucus in the pharynx and larynx which the patient could not expel. There was great difficulty in articulation in Case 2. Paralysis of the trapezius and sterno-cleidomastoid muscles or of the deep muscles of the neck was not observed. The spinal accessory (eleventh) nerve may have been involved in the pharyngeal paralysis. Paralysis of the hypoglossal (twelfth) nerve appeared in two cases shortly before death. Paralysis of the diaphragm, as evidenced by total absence of abdominal breathing, was observed in Cases 6 and 7 towards the end of the illness. It may have been overlooked in the others. The patients at that time breathed heavily but not over 28 per minute, and the accessory respiratory muscles were in play. They complained of suffocation and lack of air, but there was no cyanosis of lips or face. Whether the paralysis was due to injury to the phrenic nerve or to interference with the respiratory centre is doubtful. Inco-ordination was not observed.

A general convulsion occurred in Case 5. It was severe but of short duration and did not recur.

With one exception, the mentality was clear in all the patients until shortly before death, when drowsiness and inattention to environment appeared. Patient 6 had a period of coma on the last day, lasting two to three hours, from which she partially rallied. Patient 1 was described by her physician as hysterical, which condition was attributed to a domestic misunderstanding of a few hours before.

The temperature was normal or subnormal in all cases except following serum administration in Case 7, and shortly before death in Case 2. The respiration was below 30 in all cases in which it was noted. The pulse was rapid and variable in rate, a little exertion or anxiety sending it as high as 130 to 150 per minute. The general physical examination was negative in all cases except 6, in which there were râles at the base of the lungs a few hours before death.

Urinalysis in two cases was negative. Blood counts were not made. One nurse noted a peculiar sweetish odour in the stools of three patients.

The termination of illness came with great weakness and collapse, slowing and diminution of respiration, and a rapid, weak pulse. The heart continued to beat after the breathing had ceased.

Diagnosis. Two points stand out: First, cranial nerve paralyses are constant symptoms in food poisoning due to *B. botulinus*; they frequently precede the gastric symptoms, and they may constitute the whole clinical syndrome. Second, the time of onset of symptoms varies to such an extent that the poisoned individuals may scatter widely and the presence of an outbreak may not be recognized.

The first patient to be taken ill, Case 1, was not observed by the analysts and her illness was unknown to the family until, seeing the report of the death of the boy in the papers, her relatives called up. Her physician was puzzled over the case and suggested poisoning, but his suspicions were not aroused enough to demand a necropsy.

The cause of illness in the second patient was also unrecognized. A diagnosis of pseudobulbar paralysis was made on the evidence of the paralysis of the third, seventh, tenth, and twelfth cranial nerves, the first two showing right-sided lesions. The aetiology of the condition was obscure because the patient was in excellent health and presented no evidence of cardiovascular disease or syphilis. A bulbar palsy of infectious origin was ruled out by the absence of fever, and similarly a diagnosis of acute poliomyelitis with bulbar symptoms was discarded. Because of the rapidity of the course, progressive muscular atrophy of the bulbar type and myasthenia gravis were not considered. Poisoning by belladonna, hyocyamus, or gelsemium were impossible because the patient had not taken any of these drugs. The unsatisfactory conclusion was finally reached that cerebral thrombosis and softening were responsible for the condition.

When, subsequently, the boy and the maid in the home of Mr. M. W. S. were affected almost simultaneously with gastro-intestinal and neurologic symptoms, the presence of food poisoning was recognized and the diagnosis of the two previous cases was cleared up.

All the genuine outbreaks have, as has been shown, truly monotonous common features. In none of them is there any evidence of contact infections occurring after food poisoning due to the paratyphoid bacilli. In all of them it is the food itself which is toxic, even if it had been boiled, or otherwise treated, beforehand. In all of them the symptoms indicate an acute involvement of the central nervous system comparable to the effects of poisonous alkaloids. The discovery of *B. botulinus*, exceedingly rare as it is, seems almost an epiphenomenon. In fact it is only in some portions of the food, or in a batch of which the poisonous meal formed a part, that it is found, as well as occasionally in the spleen of the fatal cases, while the search not infrequently fails if made in the various body fluids and excretions of the patients during life. It is by serological means that the diagnosis is most definitely established.

The nature and characters of *B. botulinus* are in keeping with these peculiarities of the outbreaks. Meyer and Geiger reviewing results which had been obtained from the bacteriological examination of tissues and stools in four outbreaks of botulinus poisoning, found that spleen cultures which were made in two instances were negative, while those made from stools in two cases in different outbreaks contained *B. botulinus*, Type A, on the sixth, seventh, and eleventh days following the consumption of the contaminated food. They recommend that in all cases of suspected botulinus poisoning cultures should be made from the spleen and from stools.

Morphology and biology of *B. botulinus.*

B. botulinus is a very elusive species. Outside the related instances of food poisoning it has been found to be widely disseminated in nature. Kempner and Pollack isolated it in 1897 on a single occasion from the faeces of a pig in Berlin. This bacillus was found by van Ermengem to be more closely related to the Darmstadt strain than to the original Ellezelles virus, but the discoverers claim to have obtained a specific antiserum for it which neutralized both the Darmstadt and the Ellezelles toxins. Van Ermengem failed to isolate the bacillus from 52 different materials abundantly contaminated by anaerobes, such as faeces of domestic animals, intestinal contents of fish, soil, sewage, &c. The examination of the historic Ellezelles pigsty, where the first strain was isolated, was also of no avail.

Dickson followed up the work of Kempner and Pollack. He examined the contents of the colon and ileum of 250 grain-fed hogs which were slaughtered for market in south San Francisco. *B. botulinus* was not found in any instance, which leads to the supposition that this organism is not a normal inhabitant of the intestine of grain-fed hogs. Similarly *B. botulinus* was not demonstrated in ten samples of manure from two groups of garbage-fed hogs.

Dickson also failed to find *B. botulinus* in samples of soil from two gardens in which, in the summer of 1917 beans had been grown which in early 1918 caused two outbreaks of botulism. Burke, as a result of numerous experiments, found that *B. botulinus* was widely distributed in nature. Two hundred and thirty-five cultures were made from samples collected in five localities in central California, 50 or more miles distant from each other. The cultures covered a wide range of material, including tap-water, hay, leaves, vegetables and fruits in various conditions, insects, spiders, sow-bugs, snails, and caterpillars, garden soil, manure from horses, hogs, and chickens, and also samples from the claws and beaks, and crop, gizzard, and intestinal contents of birds.

B. botulinus is present in garden soil, and may contaminate fruit or vegetables; it is not necessarily associated with active decay, but may be present in the damaged skin of apparently sound fruit and vegetables.

It was found in the faeces of a hog four months after contaminated food had been eaten.

Finally it must be remembered that *B. botulinus* may be found not far from human habitations. Of the five localities visited by Burke only one failed to give positive results as to the presence of *B. botulinus*. This one, Madera, differed from the other four in being isolated and deserted.

B. botulinus is not easily isolated from some materials containing it.[1] The difficulties consist in picking it out from the various anaerobes which usually co-exist in 'botuligenic' products or organs obtained on post-mortem examination.

Morphology. B. botulinus is a large straight rod measuring from 4–6 μ in length by 0·9–1·2 μ in breadth with rounded ends. The bacilli are either single or in twos or threes in a chain, rarely more. Involution forms are said to be common in artificial media, but this observation is probably based upon experience with impure cultures. The organism is Gram-positive and slightly motile, possessing a few (4–8) peritrichal cilia. Oval spores are formed in all media, are sub-terminal, and produce slight distension of the rod. It has been stated that sporulation occurred most readily at from 20° to 25° C., and is usually absent at higher temperatures. The process occurs, however, as readily at body temperature, and there is usually some evidence of commencing sporulation after 24–48 hours' incubation at 37° C.

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[1] The suspicious food, e. g. ham, is either minced and an emulsion made of it, or small disks or cubes cut out and plates of gelatine-glucose or glucose broth inoculated. The food is not usually tainted, and the bacilli are not evenly distributed throughout the article examined. In the case of ham the bacilli, as a rule, agglomerate in the fat, particularly along the bone. A rancid smell is indicative of their presence, but it is not easy to detect by naked eye the rancid parts of fat. Bürger recommends that a disk of ham be placed into a copper sulphate, copper acetate, or a copper-chrome-alum-acetic acid mordant, in which the rancid portions will take a greenish colour. It is in these parts that the majority of bacteria will be found.

B. botulinus may be readily isolated from agar transplants made direct from the contents of cans of spoiled food, because there are, as a rule, few other bacteria present (Burke). In the case of such materials as manure, intestinal contents, &c., in which other strict sporing anaerobes are present, usually in much larger numbers than *B. botulinus*, the process of isolation presents considerable difficulty. Burke recommends primary inoculation of such material in Van Ermengem's broth and chopped meat media, in duplicate. One set is heated for one hour at 60° C. in order to remove non-spore-bearing organisms, and the cultures are incubated at 28° C. The presence of *B. botulinus* in the cultures is determined by the presence of the specific toxin. Small quantities are filtered, and 1 c.cm. of the filtrate is injected subcutaneously into a guinea-pig of about 250 grm. weight. If the animal dies within four days the filtrate is tested against both types of antitoxin (A and B) of *B. botulinus*.

Such a test determines the presence or absence of *B. botulinus* and also the type.

The organism is isolated from broth or meat cultures in which the specific toxin is demonstrated. Instead of the usual anaerobic plate methods, Burke prefers to use thinly seeded agar shake cultures. After incubation these are examined and fished by transmitted light on the stage of a dissecting microscope, such as is used for zoological work, having a lens with a magnifying power of 10–20 diameters.

Cultivation. Shake or stab glucose-agar cultures, show abundant gas production, with the consequent fragmentation of the medium; coagulated serum is not liquefied. McIntosh reports that, in addition to the fermentation of glucose, 'distinct quantities of acid were formed in maltose, lactose, glycerine, and starch'. In milk the growth is scanty and no change is produced.

The optimum temperature was, until recently, considered to range between 25° and 30° C. Orr and others have shown, however, that the optimum temperature for growth and toxin production is 37° C. Growth is usually apparent at the end of 24 hours at 37° C., or 36 hours at 28° C.

B. botulinus is an obligate anaerobe, and requires glucose or animal tissue for its growth. It can also grow in the presence of oxygen in symbiosis with certain aerobic species as, for example, staphylococci or *B. subtilis*, a fact which probably explains its being found on the surface of some articles of food. For laboratory purposes the most suitable medium consists of ordinary broth containing a small quantity of autoclaved minced meat. In such a medium growth is usually evident within 24 hours. All cultures of *B. botulinus* exhibit a peculiar rancid odour which is quite distinct from the putrid smell of many other anaerobes.

It is a proteolytic organism, and digests and darkens meat and brain media, but does *not* produce blackening. Reddish found *B. sporogenes* as a contaminant in 18 of 19 strains obtained by him from different laboratories in U.S. This may explain the differences in the description of *B. botulinus* made in the U.S. and by European investigators. Similarly, the use of such impure cultures in the preparation of antitoxin may account for some of the unsatisfactory results in treatment.

Deep agar colonies, seen under the dissecting microscope with a magnification of 10–20 diameters are *very characteristic* (Burke). In young cultures 'the typical colony is a thin, translucent disk, having a small opaque knot or nucleus on or near the periphery at one side. The edge of the disk is either flattened or sharply indented at the point nearest the knot. The disk is more or less completely filled with clear spots or "vacuoles" which are in reality gas bubbles caught in the meshes of the bacterial growth.' Such colonies are diagnostic of *B. botulinus* as is also the fact that after from 3 to 6 weeks' cultivation the disks remain transparent.[1]

Viability persists for much longer periods in meat and brain media than in ordinary broth or agar. Wyant and Normington as a result of the study of 19 strains of *B. botulinus* in alkaline media (reaction 0·5) with NaCl in concentrations of 1%–10% found considerable variations in the viability of the organism after various periods of time. Five strains of low, 5 of high virulence, and 4 others were still viable after 27–48 days in 10% NaCl; 3 virulent strains survived 11 days, but less than 31 days in 10% NaCl solutions. Inhibition of *B. botulinus* in salt solutions up to 10%, which has been described by other workers, is probably not concerned with the NaCl so much as with the reaction of the culture media.

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[1] The heavy hairy tuft exhibited by the illustrations of V. Hibler's cultures, likewise the changes taking place in milk media, were doubtless due to impure cultures.

Resistance of spores. Weiss examined emulsions of the spores of 16 strains of *B. botulinus* in a medium composed of 2 parts of finely ground sheeps' brains and 1 part of water. After being exposed in 6″ × $\frac{3}{4}$″ tubes for varying periods of time in a De Khotinsky oil bath at 95° C., 100° C., 105° C., and 120° C., the following important observations were made:

(*a*) The spores are destroyed within 5 hours at 100° C., within 40 minutes at 105° C., and within 6 minutes at 120° C.

(*b*) The spores are killed gradually, suffering injury before their destruction.

(*c*) Spores one month old are three times as resistant as those 5 months old.

(*d*) The more concentrated emulsions of spores resist higher temperatures than do less concentrated emulsions.

(*e*) NaCl lowers the resistance of the spores.

(*f*) The hydrogen-ion concentration also has considerable influence on the thermal resistance. In acid or alkaline media of P_H above or below 7·0 the resistance to heat is greatly reduced.

'It is evident therefore that the determination of the P_H just before sterilization of canned foods, and the allowance of a safety factor in the time of heating, are necessary as precautions to be observed in all practical processing methods.'

Types of B. botulinus. Two types of *B. botulinus* are recognized, and have been named respectively A and B. Morphologically they are indistinguishable, and can only be differentiated by the toxin which they produce. Antitoxin which has been produced by the toxin of Type A is incapable of neutralizing the toxin of Type B, and the converse holds good. Certain animal inoculations may be employed for the differentiation of the two types, but the most satisfactory method is by means of the known specific antitoxin.

Toxigenic properties of *B. botulinus*.

However precise all these details of the growth of *B. botulinus* may be they would not suffice to identify the bacillus specifically. It is the peculiar toxicity which marks its individuality.

Cultures of *B. botulinus* as well as the bacteria-free filtrates produce in animals symptoms identical with those following the administration of the poisonous food which had caused botulism in man.

Toxin is readily produced in suitable media at 37° C. The period of time required for the maximum production varies according to the nature and reaction of the medium. In 2 per cent. peptone broth containing a small proportion of minced meat and with a P_H concentration of 8·2 the maximum toxin content is obtained after 5–7 days incubation at 37° C. The *average* M. L. D. of such a toxin for a 250 gramme guinea-pig varies from ·0001 to ·00001 c.cm. It is unnecessary to adopt any special means of obtaining anaerobiosis in the case of large volumes (2–4 litres or more), but it is advisable to place the inoculum at the bottom of the container.

Rapidity of toxin production is facilitated, in the case of large volumes of medium, by incubating for 24 hours at 37° C. prior to inoculation. After the fifth day of incubation small samples may be filtered daily and tested for the toxin content. A useful and rapid preliminary test consists of injecting the toxin intraperitoneally into mice. When quantities as small as ·01 to ·001 c.cm. injected in this manner produce symptoms within two hours and death within six hours it may reasonably be assumed that the guinea-pig M. L. D. (that is the smallest amount which, if injected subcutaneously will kill within 96 hours) is at least 100 times greater. Toxin of such a titre is quite suitable for all ordinary experiments and for immunological purposes.

Toxic by-products. Bronfenbrenner, Schlesinger, and Orr observed that mice receiving gradually increasing quantities of botulinus toxin frequently died within a few minutes of receiving an injection of 0·5 c.cm. of filtrate. It was found that this rapid death was due to poisonous products other than the specific toxin, which are not neutralized by the specific antitoxin and are not precipitated by alcohol, but are dialysable and thermostable. These substances have been regarded as of importance inasmuch as they may introduce a source of error in connexion with the examination of partly decomposed food products when toxins are suspected, but their importance has probably been exaggerated, since the potency of the toxin in contaminated food material is of such a high order that the quantity of inoculum for test purposes would not contain sufficient of the products to produce an effect. Similar substances have been observed in cultures of atoxic strains of *B. sporogenes*, *B. tetani*, *B. proteus* and other organisms when these were grown in a medium containing minced meat.

If antitoxin is not available for neutralization tests these substances may be detected by their thermostability.

Thermostability of toxin. Orr, working with the toxin produced by ten different strains of *B. botulinus*, found that the wide variation in heat resistance shown by the different strains was unrelated to their potency. The toxin produced by one (Nevin) was found to be much more resistant than that of the others. There was no apparent correlation between the resistance of the toxins and their type, as determined by toxin-antitoxin tests. All were found to be comparatively thermolabile.

At 80° C. they were destroyed in from ½– 5 minutes.
„ 70° C. „ „ 2–18 „
„ 65° C. „ „ 10–85 „

The average temperature coefficient of the destruction of the toxin on increasing the temperature from 65° to 72° was found to be 5·2. On increasing the temperature from 72° to 80° the average temperature coefficient was 4·2.

Precipitation of toxin by alcohol. The toxin of *B. botulinus* is rapidly destroyed by ethyl alcohol. As shown by Bronfenbrenner and Schlesinger even weak solutions (20 per cent.–30 per cent.) destroy many thousand lethal doses *in vitro* in from 5–16 minutes at 37° C. In this respect, therefore, this toxin is unlike tetanus or diphtheria toxins. In several outbreaks of botulism it has been shown that persons who had taken alcohol with their food were not so badly affected as were those who had not drunk alcoholic beverages. This fact has been confirmed experimentally in guinea-pigs. Of two groups of these animals, one of which received toxin alone while the other had toxin together with alcohol, those of the first group died while the latter survived. It has been definitely shown that alcohol possesses a destructive effect upon the toxin only when in direct contact, for if toxin is given by the mouth and large doses of alcohol are injected subcutaneously, or if alcohol is given by the mouth and toxin is injected intraperitoneally, the action of the toxin is not affected.

Action of toxin on living tissues. As a result of experiments carried out in dogs, cats, and rabbits, Dickson and Shevky found that the toxin did not impair the upper and lower neurons of the skeletal motor nerve supply, or disturb the spinal reflex arcs of the extremities. The nerve impulses were blocked in the nerves of the non-sympathetic portion of the involuntary nervous system, for example, the vagus, the chorda tympani and the nervi erigentes. Apparently the blocking is of a temporary nature, relatively unstable and not due to destruction of the nerve elements.

Semerak has described the pathology of a fatal case of human botulism in detail and concludes that the changes are confined to the vascular system. Thrombosis of arteries and veins is the initial change, followed by ischaemic necrosis and later by inflammation. He considers that the toxin has no direct action on nerve cells, the retrogressive changes being secondary and due to the disturbed blood-supply. The ganglion cells of the motor cranial nerves are always involved because their blood-supply is derived from terminals of branches of the vertebral arteries which appear to be the seat of predilection of the thrombosis.

Differentiation of the two types of toxin. B. botulinus differs from all other toxin-producing organisms in that it possesses two distinct types which have been named respectively A and B according to the toxin which they produce. Morphologically, culturally, and indeed in all other respects, these types are quite indistinguishable. They can only be differentiated with certainty by titration of their respective toxins against the specific antitoxin. Type A antitoxin is capable of neutralizing its homologous toxin but not toxin of the other type: the same holds good in the case of Type B antitoxin.

Graham and Schwarze had observed that experimentally chickens were susceptible to Type A and highly refractory to Type B toxin, and suggested therefore that these animals might be used for the differentiation of the toxins. When the specific antitoxins are available, however, they should always be employed.

The **effect of the toxins** differs according to the way of their administration, and it will be more convenient to consider separately the modes of injection.

(1) *Subcutaneous injections.* Quantities as small as ·00003–·0001 c.cm. of a glucose broth culture will kill a rabbit in 36 to 48 hours with symptoms of a general or local motor paralysis of varying intensity. The paralysis may involve only certain groups of muscles; the head inclines to one side, the forelegs are extended, the hind legs contracted towards the abdomen. In such a position the animal will remain until death supervenes. In other cases only the hind legs will be paralysed and the animal will painfully creep on its forelegs, with its tail stretching outwards. An intense salivation, mydriasis, flaccidity of the third eyelid, exophthalmos, aphonia, complete anorexia with retention of urine or faeces are almost constant features. The symptoms come on suddenly, but in some cases there is an incubation of

3 to 4 days and they do not appear until a few hours before death, which is preceded by clonic convulsions and pitiful squealing.

Guinea-pigs are particularly susceptible, ·0001 to ·00005 c.cm. often sufficing to produce a total paralysis of all muscles so that the whole body appears completely flat. The animals remain motionless with outstretched limbs. The respiration is at first quick or superficial and then it slows down. The intercostal spaces contract inwards and attacks of dyspnoea follow, the animals dying within 18 to 36 hours, or with smaller doses—in 3 to 4 days. Should the animals resist longer various paralyses will be noted such as, for example, of the hind legs or a prolapse of the penis which can persist for weeks. The earliest and most characteristic symptom consists in the loss of resistance of the abdominal muscles (Madsen's phenomenon). This is rapidly followed by salivation and loss of voice.

If the injection be made into a limb, one sometimes observes a condition similar to local tetanus, i.e., the paralysis of the limb supervening after 20 hours (Leuchs's observation).

Mice vary in susceptibility. In some instances a trace of the toxin will kill with paralysis of the hind legs as the characteristic symptom. In others individual mice show a relative degree of resistance. For this reason these animals are unsatisfactory for test purposes.

Small monkeys (*Rhesus*) will react in a very characteristic manner to an injection of ·01 to ·001 c.cm. of the culture. There will be: pupils markedly dilated, and often immovable, bilateral ptosis and fixed vision, abundant greenish discharge from mouth and nose causing attacks of cough and dyspnoea, complete aphagia, followed by dyspnoea and death in 24 to 36 hours.

Cats represent the experimental animal *par excellence*. The neuro-paralytic symptoms produced may be described as pathognomonic. Most marked mydriasis with an immovable iris, complete paresis of the third lid with fixed eyeballs, aphonia, aphagia, marked prolapse of the tongue persisting at times for weeks, abundant mucous discharge from the throat and mouth, croupy cough, complete retention and general muscular asthenia—this is a picture produced by ·1 to 1 c.cm. of the toxin which will usually kill in 6 to 8 days. Large doses are followed by a latent period of 6–12 hours, after which there develops a general paralysis, the animal dying in collapse within 16 to 24 hours. Small doses, e.g. ·01 c.cm., will induce a cachectic condition which may drag on for weeks or months.

White rats are not susceptible. Dogs are said to resist enormous doses (10 to 30 c.cm.) with no more reaction than passing fever and loss of weight. Fowls are resistant to Type B but readily succumb to Type A.

Pigeons will react to an injection of ·1 to ·5 c.cm. into the breast muscles in a typical manner, namely, a more or less complete paralysis of the wing muscles, complete ptosis, and regurgitation of masses of a greenish fluid will be observed. The birds cannot move, and die in a few days.

(2) *The intraperitoneal injections* of similar quantities of toxin produce a more rapid effect than do subcutaneous injections.

Dyspnoeic symptoms are easily induced; they appear early and will follow even slight doses. The same applies to intrapleural injections.

It seems likely that the toxin acts on the nerves of the diaphragm, thus producing its paralysis. (Forssmann).

(3) It is very striking that *intracranial* and *intracerebral* injections

are not followed by any earlier appearance of, or any more marked, symptoms than intraperitoneal or subcutaneous injections.

This is in marked contrast with the behaviour of the tetanus toxin, a fact which will be commented upon presently.

(4) *Intravenous injections* are particularly fatal to goats or horses, a fact of importance for the preparation of antitoxic sera. In other animals much the same acute symptoms are produced as follow large doses in subcutaneous injections. The effect on mice is worth noting. Quantities so small as ·00001 to ·000003 c.cm. of a 14 days old culture will kill a mouse of 15–20 gm. in 20 to 30 hours.

(5) *Intra-ocular injections* are of peculiar interest in view of the ocular symptoms which form such a characteristic feature of the disease. The ophthalmoplegic symptoms do not appear any sooner after an intraocular injection, the reaction of the untreated eye developing in its proper time. The mydriatic properties of the toxin differ thus from those of atropine, being solely dependent on central disturbances.

(6) *Intoxication by ingestion.* This is a most characteristic feature of the botulinus toxin and differentiates it from other bacterial toxins and from the serpent venom. Monkeys, guinea-pigs, and mice fed with the toxin will react in the same typical way as after injections.

Rabbits are more resistant to the ingestion of the toxin, 5 to 10 c.cm. representing the fatal dose as compared with ·00003 to ·0001 c.cm. in subcutaneous injection. If the toxin be introduced into the large bowel or the caecum the rabbits will not succumb even to a 2,000 multiple of the subcutaneously fatal dose.

Monkeys, however, will be fatally poisoned by the ingestion of very small doses, while a drop or two of toxin given on a piece of bread will kill a guinea-pig in 24 to 36 hours.

Cats will withstand enormous doses of the culture or of the toxic food without showing the slightest symptoms. Prolonged feeding with the toxin may, however, succeed in inducing transient paretic symptoms, muscular weakness, gastro-intestinal reactions, and may ultimately bring about marasmus.

Dogs will not react in any way, even to the most massive doses of toxin in food.

Experiments which have recently been carried out by Bronfenbrenner and Schlesinger explain to some extent the phenomena observed when this toxin is taken by the mouth. It was found, for example, that the lethal dose of toxin by the mouth is about 1,000 times as much as the intraperitoneal M. L. D. This holds good for all laboratory animals, including birds.

Toxin purified by precipitation retained its full potency when tested by injection, but became 100 times less toxic by mouth. The purer the toxin the less toxic it became per os. The addition, however, of substances removed during the process of purification increased the toxicity of the purified toxin. They therefore concluded that 'the power of crude botulinus toxin to be absorbed through the intestine is dependent upon the presence of secondary substances mixed with the true botulinus toxin' As a result of further experiments, they found that the relation between the size of the M. L. D. per os of precipitated toxin, and that by intraperitoneal injection of the original toxin is 1,000 : 1. If, however, the precipitated toxin is redissolved and similarly tested, the relationship is 100,000 : 1. That is to say, while the toxicity by injection remains unchanged, the toxicity by mouth decreases 100 times as a result of the precipitation of the toxin. The addition, however, of suitable amounts of the fraction soluble in saturated ammonium sulphate restored the toxicity per os.

The authors suppose that the toxicity of the crude toxin by mouth is due, at least in part, to the increase in permeability of the digestive tract, and that the fraction soluble in saturated ammonium sulphate contains substances which are capable of influencing this permeability.

As a result of earlier experiments it was evident that the toxin was not destroyed by the acidity equal to that of the stomach. It was found, moreover, that the potency of the toxin during active digestion was greater than in the empty stomach, and this was ascribed to the increased acidity during the process of active digestion. It was subsequently shown that by adjusting the reaction of a toxin of which 3×10^{-6} c.cm. represented a mouse M.L.D. to a P_H of approximately 4·0, the M.L.D. became 3×10^{-18} c.cm. and occasionally 3×10^{-21} c.cm. That this increase in potency was due to acidification was shown, since the correct neutralization resulted in its returning to the original titre, and further, that readjustment of the reaction to $P_H = 4{\cdot}0$ resulted in the restoration of the potency of the first acidification.

As the culture of *B. botulinus* grows older the crude toxin assumes a more stable form which is less readily changed by acidification.

It is interesting to note that the neutralizing value of the homologous antitoxin is unchanged—that is, the amount required to neutralize 100 lethal doses of the crude toxin is capable of protecting against many million lethal doses of acidified toxin. Moreover, the dose of such acidified toxin required to kill per os is as great as the dose of crude filtrate from which the high potency toxin was prepared. The authors conclude that 'since the potency of acidified toxin is again reduced when it is neutralized (as would occur in the small intestine), it seems likely that botulinus toxin is absorbed to a large extent from the stomach and upper duodenum'. These interesting observations have not yet been confirmed.

Antitoxin. The first attempt to produce horse antitoxin on a large scale was made by Leuchs in 1909. Ornstein has since immunized horses in 1911 and 1912 at the Berlin Institute of Infectious Diseases, and this antitoxin is at present in use—though said to be difficult to obtain—in Germany.

The earlier attempts of Kempner (1897), Forssmann (1900–2), and Wassermann (1905–7) aimed at the immunization of goats, and these authors had obtained potent protective and therapeutic sera.

All these antitoxic sera were thoroughly tested on animals. They neutralized their homologous toxins, they protected, and even 24 hours after the injection of a lethal dose, they cured even when the first symptoms had appeared, providing the dose of the toxin was not too high (they were of no avail against 10 lethal doses).

More recently antitoxic sera of both types have been prepared in America and in this country. Given a toxin of reasonable potency (g. p. M. L. D. ·0001 to ·00001) no difficulty is experienced in the production of an antitoxin of such a value that ·00001 to ·000001 will protect a guinea-pig against 100 M. L. D. of toxin when the mixture is injected subcutaneously. The antitoxin is readily obtained by the hyper-immunization of horses on similar lines to those adopted in the preparation of diphtheria or tetanus antitoxin. Horses are highly susceptible to botulinus toxin: quantities as small as ·1 c.cm., being capable of producing fatal symptoms when injected subcutaneously. Relatively few horses appear to possess a normal antitoxic content. The preliminary injections should consist of mixtures consisting of 10 c.cm. or more of 50 % over-neutralized toxin. Subsequent injections consist of mixtures in which the proportion of antitoxin is gradually decreased until a preliminary injection of un-neutralized toxin is given. The quantity of crude toxin is then increased at suitable intervals until the maximum response is obtained.

Standardization. The method of standardization of botulinus antitoxin employed by Bengston and others in America and recognized in this country is as follows :—A standard antitoxin is used to determine the test dose (100 M. L. D.) of the corresponding toxin which is in turn titrated against the unknown antitoxin. *The minimum amount of antitoxin which is capable of protecting a* 250 *gm. guinea-pig against* 100 *M. L. D. of such a toxin for* 96 *hours, when injected subcutaneously is regarded as being equivalent to one-tenth of a unit.*

For purposes of standardization a dried toxin is prepared by saturating crude toxin with ammonium sulphate. By this means the toxin is salted out and may be skimmed from the surface. After drying over sulphuric acid it is ground to a fine powder and stored in vacuo in the cold and dark. The M. L. D. of such a toxin for the guinea-pig (250 gm.) is usually in the neighbourhood of ·0000001 gm.

For the standard antitoxins the most potent serums of each of the types are mixed with glycerine in the proportion of one part of serum to two parts of glycerine. Such mixtures have been found to be very stable.

The standard antitoxin of the Hygienic Laboratory, Washington, Type A = 2·5 units per c.cm., Type B = 1·25 units per c.cm.

Testing. The antitoxin to be tested is compared with the standard unit by means of a test dose of toxin; any toxin which is several weeks old may be used for this purpose; this test dose of toxin is chosen so that, when mixed with a one-tenth unit of the standard antitoxin and injected subcutaneously into a 250 gramme guinea-pig, the guinea-pig will die within 96 hours. The amount of the unknown antitoxin which when similarly mixed with the test dose of toxin will protect the 250 gramme guinea-pig for 96 hours therefore contains one-tenth unit. Before injection the doses of toxin and antitoxin are thoroughly mixed and kept at room temperature for one hour to permit of complete combination. With every test of an unknown antitoxin two control guinea-pigs should be used, one receiving the test dose of toxin together with one-tenth unit of standard antitoxin and the other the test dose of toxin only.

Diagnosis and treatment with antitoxin. The benefits to be derived from treatment of botulism with antitoxin depend upon early diagnosis, probably even before the appearance of respiratory symptoms (Forssmann), although others (Kempner, Dickson, and Howitt) have shown that, experimentally at least, the application of antitoxin may be efficacious up to 24 hours after the injection or ingestion of *botulinus* toxin.

In actual practice it is abundantly evident that successful treatment depends entirely upon early *clinical* diagnosis. Confirmatory laboratory diagnosis of the contamination of suspected food-stuffs with *B. botulinus* is obviously of equal importance, as is also that of the particular type of toxin responsible for the symptoms.

When antitoxic sera of the two types are available little difficulty is experienced. The rapid method of diagnosis by Orr, now generally employed, quickly substantiates the clinical diagnosis. The test is based upon the observation that the intraperitoneal injection of 100 M. L. D. of *botulinus* toxin in mice produces marked symptoms within 2 hours, and death within about 6 hours. Since food-stuffs contaminated with *botulinus* toxin are usually highly toxic, this observation is of practical importance. The test consists in the intraperitoneal injection of mice with about 0·5 c.cm. of a filtrate of the suspected food-stuff. Three groups are used. Two consist of several mice each of which has received a previous injection of Types A and B antitoxin respectively. The third group, consisting of a similar number to the former two, has received no antitoxin. Twelve hours later all the mice receive 0·5 c.cm. of the suspected filtrate intraperitoneally.

If Type A toxin is present in the suspected material the mice which had previously received Type A antitoxin will survive, while those in the two other groups will succumb in about 6 hours. Similarly Type B toxin can be detected, while if the cause of the poisoning is not due to *botulinus* toxin all the animals succumb. Valuable time is saved by employing such a test before a serious attempt is made to diagnose the presence of *B. botulinus* bacteriologically.

Still further saving of time may be effected by mixing a similar quantity of filtrate with Type A and Type B antitoxin respectively and injecting the mixture intraperitoneally into mice 30 minutes later, a third or control group receiving filtrate only. In this case a definite result may be obtained within about 7 hours.

As previously stated, Graham and Schwarze used adult chickens as a preliminary method of determining the type of *B. botulinus*, but since it has been shown by Dickson that Type B is also capable of producing limber-neck in chickens, it is obvious that the only reliable method of diagnosis is by means of the antitoxin tests.

There seem to have been but a few recorded observations on the antitoxic treatment in man. In Dorendorf's case 20 and 25 c.cm. of the Ornstein serum were given intramuscularly on the 9th and the 10th days of the disease after all the ophthalmoplegic symptoms had fully developed. There was ophthalmoplegia interna totalis with a normal disk, complete incontinence, bilateral facial paralysis, complete aphagia, and painful parotitis. On the second day after the injection the mimical innervation of the face was re-established (the patient could whistle), the movement of the eyes became much freer; the paralysis of the palate was receding. On the following day the movements of the eyes were still freer, the palate was almost normal, the paralysis of the pharynx had disappeared, the patient was able to drink, parotitis was receding. On the following days the improvement continued, and eventually there was complete recovery.

Another case was given 20 and 25 c.cm. of the serum on the 12th and 13th days of the disease when the patient was in a desperate condition. The patient died 3 days after the second injection, but the serum had the same immediate local effect as in the first case.

There is therefore no doubt as to the therapeutic effect of the serum, if given sufficiently early. It is an almost unique antitoxin in the medical literature for, extremely limited as its application has been, it has been examined experimentally in minute detail with the benefit of the knowledge gained in the study of the 'standard' toxins such as the tetanus or diphtheria toxins or the cobra venom. Thus it has been shown that it conforms with the 'Morgenroth's reaction' observed for the cobra and diphtheria toxins, i.e., that acids prevent the neutralization of 'botulin' in a toxin-antitoxin mixture and liberate it from a neutralized solution. On the other hand, the 'Wassermann's phenomenon'[1] observed in tetanus remains negative, an interesting fact suggesting that 'botulin' does not travel along the nerves like the tetanus toxin.

There are, however, some distinct characteristics of the 'botulin'. The most peculiar feature is, of course, its toxic action from the stomach, which differentiates it from practically all the other toxins with the exception, however, of ricin. It is said that if a neutralized mixture of 'botulin' plus its antitoxin be introduced into the stomach, it will prove lethal unless a very great excess of the antitoxin be given. For example, if 0·00005 c.cm. of antitoxin protects against a lethal subcutaneous dose, 0·2 c.cm. will be required to protect against the 'stomachal' dose. Should the antitoxin be injected subcutaneously, while the botulin is introduced into the stomach then it will protect against a very high 'stomachal' dose.

The dissociation in the stomach does not seem to depend on its acid content since it occurs also when the acid is neutralized or the reaction rendered alkaline. It may be that the antitoxin is destroyed by the digestive juice, while botulin is more resistant or—more probably—the 'botulin' is more easily resorbable from the mucous membranes while the antitoxin—by analogy with the tetanus and diphtheria antitoxins—is very badly resorbed or no resorption takes place.

The term 'botulin' is of course generic. Toxins produced by different strains vary considerably in their potency, a property common to all toxigenic bacteria. There is also the usual variation due to the difference of media. Thus 'pork broth' toxins are said to be as a rule more active than 'beef broth' toxins, the ratio expressed in terms of minimal lethal doses for guinea-pigs of 220 grammes by subcutaneous injection, being, for example, $\frac{0{\cdot}0001-0{\cdot}00005}{0{\cdot}004-0{\cdot}003}$. This difference in toxicity of the media may, however, be due to some extent to the P_H concentration.

Some strains are more tolerant of the reaction of the medium in which the 'botulin' develops, than others; for example, the Ellezelles strain may produce the toxin in a neutral reaction, while the Darmstadt strain requires a definitely alkaline reaction. The *E* strain will produce a very active toxin in 14 days at 22° C., while the *D* virus will give but a feeble yield. Some toxins, again, will be more active by ingestion than others, &c. Such a variety in toxigenic properties is common to all of the known toxin-producing organisms.

But in addition to the above variations there is the fact that two distinct types are recognized, according to the specificity of their respective toxins. *Hence the original conclusion that therapeutic sera should be polyvalent.*

Pathological lesions. It has been shown that 'botulin' causes symptoms in animals which are at least comparable to those observed in botulism in man. The pathological lesions produced are also to a certain extent comparable, but unfortunately there is no unanimity as to the lesions found in man.

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[1] If a neutralized mixture of tetanus toxin plus antitoxin be injected into a guinea-pig which has received an injection of adrenalin, the resorption of the antitoxin becomes impossible in view of the supervening paralysis of the vessels, while the toxin remains at liberty to travel along the nerves.

If death takes place quickly the macroscopical changes found in the organs of the animal are insignificant; if, however, the disease is protracted, there will be hyperaemic changes, sometimes indications of necrosis and of an advanced fatty degeneration of the liver, spleen, and kidneys. If the toxin has been ingested there may be a hyperaemic condition and softening of the intestinal wall accompanied by haemorrhagic foci along the intestinal tract.

Histologically there will be found a hyperaemic condition of most of the parenchymatous organs, hyperaemic dilatation of the vessels in the liver, kidneys, stomach, and the cerebrospinal tissues, sometimes accompanied by extravasations of blood and infiltration by leucocytes.

The 'botulin' acts upon manifold cellular elements, producing a diffuse granular, fatty degeneration of the endothelium, the secretory cells of the liver and the kidneys, the muscles, &c. It attacks electively the secretory cells of the salivary glands producing therein mucous degeneration. In the brain as well as in the cranial and spinal nerves there are no lesions, but the cellular elements of the central nervous system are affected, namely, those of the grey substance of the anterior horns of the cord and of the nuclei of the medulla oblongata and pons. The lesions of the nerve cells are said to consist in the break up leading to chromatolysis and in the destruction of the Nissl bodies. This process is described as taking place in three stages: (1) a stage of diminution or even complete disappearance of the chromatophil elements, particularly of the central part of the cell; (2) the agglomeration of the Nissl bodies in groups and their subsequent powdery destruction, the cells becoming larger; (3) the formation in the interior of the cells of vacuoles; the contours of the cell become irregular, and there is an immigration of hyperplastic neuroglial elements from the periphery, the nuclei and nucleoli remaining intact. In the medulla oblongata the lesions stop at the second stage. They are fully developed in the nucleus ambiguus, the nucleus of the Xth nerve, the cells of the olives, in the nucleus medianus and the nucleus of the 3rd nerve. The glia cells are assumed to act as neurophages.

There are also haemorrhagic foci of varying extent, particularly at the bases of corpora quadrigemina.

It is interesting to note that in animals which were saved by the injection of the antitoxin, and in which the chromatolysis, &c., had already developed, all these lesions receded a fortnight after the cure of the animals.

Thus it will be seen that there is no specificity in the lesions; indeed similar changes are observed after poisoning with the diphtheria or tetanus toxins, and after infection with the hydrophobia virus. It will be noticed that no inflammatory reactions were observed, and as a consequence an elective effect of the toxin on the nerve cells has been assumed. In particular the characteristic paresis of accommodation has been explained by an electively produced degeneration of the ganglion cells seated in the region of the oculomotorius nucleus.

On the whole, however, there is often a striking contrast between the severity of the symptoms and the paucity of the anatomical findings in the ganglion cells.

Further, it is interesting to observe that the lesions described in animals do not necessarily coincide with clinical symptoms in man. Thus, for example, the marked involvement of the ganglion cells of the motor and sensory regions of the cord is not in keeping with the fact that spinal symptoms are late and rare in man and sensory symptoms are never observed.

The lesions in man are often so slight that such an authority as Oppenheim remarks that there occur cases of paralysis following food-poisoning, and more or less completely comparable to the pictures of polio-encephalitis superior, inferior, acute, and polio-encephalo-myelitis acuta, which cannot be adequately explained on any anatomical basis.

In general three types of lesion have been described in human cases, all accounts agreeing as to a general hyperaemic condition of the internal organs with an occasional fatty degeneration.

1. Bürger and Dorendorf report the finding of lesions of much the same nature as those observed in animals.

Bürger found in a case which died on the 16th day of the disease 'the ganglion cells well preserved in the cerebrum, while in the region of the oculomotorius there was a powdery destruction of the Nissl granules, an eccentric position of the nuclei, &c.'

In a case which died on the 17th day of the disease (15 days after the onset of the bulbar symptoms) Dorendorf found the ganglion cells in the cerebellum and cord intact; in the medulla oblongata, pons and corpora quadrigemina—very pronounced chromatolytic lesions; in the Nissl preparations from the pons there was hardly a single normal ganglion cell; very numerous ganglion cells in the nuclei of the vagus, oculomotorius and abducens showed an almost complete chromatolysis and destruction; in similar preparations from the region of the hypoglossus nucleus only the nuclear ganglion cells were unaltered, while all others were more or less affected. Slight chromatolytic lesions were also observed in the ganglia of the cerebrum.

Further, there were progressive changes in the glia, though rather scanty in the pons and medulla oblongata.

No haemorrhagic foci were found. There were, however, hyperaemically dilated vessels and agglomerations of leucocytes in the vicinity of the vessels in the pons and the medulla oblongata.

No other lesions were detected either in the central nervous system or in individual nerves.

The histological examination of the paretic muscles of the larynx (posticus and vocalis) showed no change from the normal.

2. Paulus who examined an advanced case of botulism with symptoms of general paralysis has found two kinds of lesions:—(1) miliary, capillary haemorrhages into the central grey cavity and into the grey substance of the cord; (2) independently of these, diffused degenerations in the ganglion cells of the central nervous system without proper inflammatory processes. The haemorrhages were seated in the region of the motor nuclei, extending into the entire nuclear region of the medulla oblongata and of the corpora quadrigemina. There was also the same extensive haemorrhagic process in the grey matter of the anterior horns in the cervical cord as well as in isolated sections of the dorsal and lumbar portions. Side by side with the vascular lesions there were extensive primary parenchymatous degenerations of the ganglion cells showing various stages of cellular degeneration,

particularly of the granular pigmented form, in the oculomotorius and abducens regions.

Thus there was in the author's opinion a combination of polio-encephalitis superior and inferior with an acute degenerative haemorrhagic myelitis or, in short, a polio-encephalo-myelitis haemorrhagica.

3. Wilbur and Ophüls bring forward an altogether new contention. They challenge the hypothesis of the specific toxic action on the nerve cells, they minimize Bürger's reference to the changes of Nissl granules observed in his case by denying any importance to the findings based on such lesions, and they insist on the paramount importance of the interference with the circulation in the meninges and, particularly, at the base of the brain. They found an extreme vasodilation of both the arteries and veins which must have had the effect of a great slowing of the blood stream as a part of general paralysis of the vascular mechanism.

The most striking features of post-mortem findings on a case which died on the 13th day of the disease was an extensive microscopic thrombosis of the right arteria vertebralis at the lower end at the medulla and extending into the arteria basillaris. There were thrombi in a few of the pial branches of the basilar artery. Many pial veins at the base of the medulla and of the pons were filled with thrombi which were also noticeable in the veins of the tela chorioidea above the corpora quadrigemina and in the posterior part of the third ventricle. All the vessels in the brain tissue were much distended and full of blood. 'Quite a few' small thrombosed vessels were found near the important nuclei; quite commonly there were small perivascular haemorrhages about the thrombosed veins. Polymorph cells abounded in the thrombi. No thrombi were found in any other organs. The Nissl granules stained unusually well, especially in the large motor ganglion cells, and they were normal in every respect.

The authors exclude the hypothesis of an embolus and they admit that the origin of the thrombosis is somewhat puzzling and cannot be at present adequately explained. So far their findings were corroborated only by Dickson who succeeded in reproducing the thrombotic condition in rabbits injected with the botulinus toxin and by Semerak.

Thus it may be said that the only distinguishing feature found by all the observers consists in the total absence of any inflammatory reaction. It must be borne in mind, however, that the chapter of pathology of botulism cannot be considered as closed because all the cases described so far were isolated instances at different stages of the evolution of the toxic process and therefore not strictly comparable with one another.

It is to be feared that just as *B. botulinus* is an elusive species, so are the pathological lesions induced in the exceedingly rare examples of classical botulism.

The pathological lesions observed, whether in man or in experimental animals, show no evidence of an invasion by a virus capable of multiplication in the body fluids. It is this fact perhaps which led some of the contemporary authors (Lewin and Guilley) to express doubts as to the connexion of any bacteria with 'botulism'. It must be admitted that *B. botulinus* is an exceptional species amongst the pathogenic organisms. It has been assumed by its discoverer, and by the subsequent experimenters, to be a saprophyte because, first, it was believed to be incapable of multiplying in the animal body, and in nutrient media at the body temperature, while a like latent period separates the inducement of like symptoms whether animals be infected with living and toxic broth cultures or with bacteria-free filtrates. It is true that *B. botulinus* had been recovered from the spleen on post-mortem examinations, but they were present in exceedingly small numbers and the recovery was more successful if the organs were kept for some days before the examination, thus giving time for the spores to germinate. Cultivation from the organs of the animals injected with large doses of live toxigenic cultures is comparatively easy, but this does not disprove the original contention, since common saphrophytes like *B. subtilis* injected in a sufficient dose may also kill laboratory animals and be recovered from the organs.

Thus the evidence does point to *B. botulinus* being an unusual species of a 'pathogenic saphrophyte'. The fact that its habitat, &c., has hitherto defied recognition and its discovery is limited almost to chance, need not necessarily militate against the recognition of its aetiological import, for its elusiveness may be due not so much to the capricious frivolity of nature as to the imperfections of the manipulative abilities of man. The bacteriological writings dealing with anaerobes are indeed permeated by a controversial spirit, and charges and counter-charges of basing results on experiments with impure cultures abound in the present-day discussions on the causative agents of gas gangrene. The technical difficulties inherent in the cultivation and isolation of anaerobes as well as the somewhat confused condition of this portion of bacteriological literature, coupled with the unspectacular reward awaiting the laboratory results, have all contributed to the fact that competent bacteriologists with a working experience of the anaerobic organisms are lamentably few, and that medical bacteriology is as a rule shy of embarking upon this unprofitable undertaking. Yet the war has brought the recognition of the vital importance of the subject, and a more profound application of the experience gained may possibly show that *B. botulinus* is but one member of a large anaerobic group with a special affinity for the central nervous tissue.

Conclusions. The fact of the genuine existence of outbreaks of food poisoning no one will deny. For the want of a better name one type of these intoxications is still designated 'botulism'. Undoubted experimental evidence has shown that certain outbreaks of botulism were due to the specific action of *B. botulinus*, but it should be clearly recognized that just as 'botulism' is not co-terminous with the concept of food poisoning, *B. botulinus* has not been demonstrated to be the causative agent of every instance of genuine 'botulism'.

The increase in the recently reported cases of food poisoning in America has been explained by the fact that the Federal Authorities have been urging the necessity of 'canning' fruits and vegetables at home as a result of the world's shortage in food. The home 'canning' cannot be as efficient as that undertaken commercially, and the probability was that spores which do not escape the professional handling would resist the efforts of the amateur. This contention has been tested by Dickson who subjected cans of fruit, vegetables, &c., contaminated experimentally with spores of *B. botulinus* to the various officially recommended methods for home canning and showed that the spores in reality did survive the process. The so-called 'cold pack method' proved to be the most inefficient. It must be assumed that the heat does not penetrate the contents of the tins evenly—a fact known for meat for a long time. An essential feature of the test consisted in the long incubation (for three weeks) of the treated jars, for the more resistant spores may be but a few and time must be allowed for their germination. It has been shown on numerous occasions that certain parts only of an infected tin or ham may be toxic, whereas the bulk remains harmless. This is consonant with the above assumption and also in keeping with the biological properties of *B. botulinus* which is very susceptible to changes in the reaction of the medium. Fortunately the botulin being thermolabile a simple boiling of the toxigenic food makes it perfectly innocuous. Hence the prophylaxis of food poisoning is as simple as the treatment of it is difficult.

However plausible Dickson's experiments are, it is not impossible that some, at least, of the American cases may not have been outbreaks of genuine botulism. The evidence of commensality is lacking in some of the publications quoted previously, or even a definite food history. Had the increased incidence been connected with the distribution of canned food from a central source one might have assumed an accidental contamination by the rare bacillus. But as the gravamen lies on the home canning one would have to assume an ubiquity of the bacillus in America comparable to that enjoyed, for example, by *B. coli* in all lands. Recent investigations have indeed shown that *B. botulinus* is very widely distributed in nature. The same reasoning may apply to any instance of a sudden and widely distributed epidemic of alleged 'botulism'. The possibility of there being a comprehensive family of anaerobic food poisoners has been alluded to and cannot be dismissed *a priori* or proved without experimental evidence. But it has to be shown first, that an alleged food poisoning is in fact due to consumption of toxic food, and secondly, that other affections of the central nervous system are excluded. Emphasis has been laid already on the great similarity of the clinical picture of botulism with polio-encephalitis of different origin, and it should be borne in mind that America has been visited by successive epidemics of the Heine-Medin disease. In view of the pleomorphism of the clinical types of the disease it is not improbable that polio-encephalitic cases were sometimes erroneously diagnosed as 'botulism'.

The chapter of the experimentation in 'botulism' cannot be considered as closed. There is urgent necessity for further work, first, in the examination of the pathogenic activities of other anaerobes conceived as food-poisoning bacteria, and secondly, for an attempt at a comparative study of all the viruses with peculiar affinities for the nervous tissue.

There should also be in every country an available supply of a polyvalent antibotulinus serum, as the only hopeful means of saving life in undoubted cases of botulin poisoning and also possibly as a useful adjuvant in experimental research on the microbial origin of various affections of the central nervous system.

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ABSTRACTS

SURGERY

Moynihan, Berkeley. The early signs and symptoms of cholelithiasis. *Brit. J. Surg.*, 1922, **10**, 127.

It has probably been the experience of many surgeons to operate upon cases in which a diagnosis of cholelithiasis has been made and to fail to find any stones within the gall-bladder. Sir Berkeley Moynihan discusses the condition which has led to this diagnosis and shows that there are several conditions of the gall-bladder, apart from calculous disease, which closely mimic the symptoms of gall-stones and can be successfully treated only by cholecystectomy. The first of these is the so-called strawberry gall-bladder, a condition in which there is a destruction of the villi with a deposit of lipoid material in the mucous membrane. There are probably different degrees of this condition, and in the later stages tiny ulcers develop on the surface or cholesterin crystals may be embedded in the walls. Later, the gall-bladder becomes fibrous and thickened throughout and stones are present. The author points out that the symptoms which we usually regard as due to gall-stones of the bladder are really due to cholecystitis, which may be due to causes other than stones.

The various channels by which the infection takes place are then discussed. He believes that it is rare for infection to ascend from the duodenum, and lays stress upon the method by which organisms may be carried to the liver through the portal stream, and points out that there are two such streams; one from the alimentary canal and one from the spleen. The latter cannot be disregarded, for in certain conditions, such as haemolytic jaundice and splenic anaemia, gall-stones are common. Although this is perhaps the more common method, it is also probable that infection not uncommonly takes place by means of the blood-stream and from the liver by way of the lymphatics. Direct infection from inflamed surrounding structures, such as a gastric or duodenal ulcer, is rare. The evidence in favour of infection by these various routes is discussed at length.

It is stated that a large number of gall-bladders show that infection begins with almost equal frequency on the mucous surface and on the peritoneal coat. Gall-stones are only found in the later stages of an infection of the gall-bladder, but it is pointed out that there is one exception to the stones being due to an infection, and this is the pure cholesterin calculus. All other stones are due to an infection and the infection may produce symptoms before the stones are formed. These symptoms are chiefly flatulence and fullness after meals and a feeling that the stomach is over-full, even when a small meal is taken; the sudden unaccountable sensation of intolerable nausea, sometimes accompanied by faintness;

a feeling of cold associated with slight shuddering; acidity; and water-brash. Their importance lies rather in their persistence than in their individual character.

The signs of early cholecystitis as recognized at operation are the presence of thick dark bile, an oedematous, turgid, and reddened mucosa, often strawberry appearance, and, later, erosions and diverticula. Small papillomata are not infrequent. A. J. W.

Sherren, J. A comparison of cholecystostomy and cholecystectomy. *Brit. J. Surg.*, 1922, **10**, 135.

The author points out that opinion has steadily changed in favour of performing cholecystectomy more widely. He quotes his own figures to show that ten years ago he only performed cholecystectomy in 29 out of 100 cases; but in his last series of 100 cases he performed it 94 times as a primary operation and in 2 more as a secondary operation.

In the hands of a skilled surgeon the immediate mortality is lower with a cholecystectomy and the after-progress is infinitely superior. He points out, however, that this is not the doctrine to preach to those whose operative interference with the biliary passages is occasional; to these the simpler operation of cholecystostomy is the safer. The disease of the gall-bladder is what should be treated, and he states emphatically that drainage does not cure chronic cholecystitis. It is only in the exceptional case where the patient is extremely ill, and where the gall-bladder is acutely inflamed or very adherent, that drainage should be performed, but even in such cases a later cholecystectomy may be required. He also lays stress upon the fact that the symptoms in the early stages are due to the cholecystitis and not to the gall-stones. Many conditions of early cholecystitis are found at operation when no stones are present. Drainage in such cases fails to cure. All need treatment by removal of the gall-bladder.

He has had a series of 184 cases of cholecystectomy carried out for the treatment of stones confined to the gall-bladder with six deaths, three of which were due to lung complications. There has been no recurrence of symptoms in any of these cases. During the same period 152 cholecystostomies have been performed, including 46 acute cases, with four deaths. Of the acute cases 8 have had a definite recurrence of symptoms. Of the 106 non-acute cases 21 have had similar relapses. In two of the cases an operation had to be performed upon recurrences as late as seven and nine years after drainage. In addition to the recurrences, 5 patients died within four years of carcinoma, certainly or probably of the gall-bladder. Thus, out of 148 there were 34 in whom the result was unsuccessful after a period of years.

He sums up by saying that cholecystectomy is safer for the patient, the risk of recurrence is negligible, and the loss of the gall-bladder interferes in no way with his well-being. A. J. W.

Rowlands, R. P. The relative merits of cholecystectomy and cholecystostomy. *Guy's Hosp. Reports*, 1921, **71**, 454.

According to Rowlands, the more the natural history of the gall-bladder is studied in association with disease the more it comes to be regarded as a useless and troublesome vestigial organ. Various animals get on well without it, and its removal in man is not followed by any serious effects. The question of the comparison of cholecystectomy and cholecystostomy can be conveniently discussed under two headings, according to whether the disease is limited to the gall-bladder or not.

The author quotes Mayo's statistics from 1907–1916 to show that cholecystectomy is no more dangerous than cholecystostomy, for in 2,493 cholecystectomies the mortality was 1·3 per cent. and in 2,854 cholecystostomies it was 1·5 per cent. The convalescence and ultimate results of cholecystectomy are more satisfactory in every way. After cholecystostomy recurrence of symptoms and secondary operations are infinitely more common; for the primary disease, generally infective in nature, is in the walls of the gall-bladder and has been shown by Rosenow to persist indefinitely after drainage. Another reason for its removal is that it may be the seat of early malignant disease, which may only be discovered by microscopical examination after removal. In such early cases the prognosis is good. He quotes a patient who remained well ten years after such an operation.

Sometimes, however, cholecystectomy may not be so easy or so safe an operation. Hence if the patient is very ill, old, or feeble, and the gall-bladder is much inflamed, the surgeon, especially if he is not very experienced in this branch of surgery, will be wise to choose cholecystostomy. Incidentally it is right to say that the surgery of the bile apparatus is not to be lightly undertaken by the amateur or the novice.

In the second group, when the disease is not limited to the gall-bladder and cystic duct, there is more room for doubt, for it is evident that the gall-bladder should not be removed unless it is certain that the common bile-duct is patent and likely to remain so. It is too risky when the patient is very ill, old, or feeble, and especially in the presence of long-standing jaundice. He also states that no one would suggest the removal of the gall-bladder when infective cholangitis exists, for in this grave condition the only justifiable operation is the removal of stones and the drainage of the common bile-duct. (All surgeons will, however, not agree with this statement. It is often easier and simpler to remove the inflamed gall-bladder and to drain the common duct through the cystic duct rather than to drain the gall-bladder and make a separate incision in the common duct.) He states that in favourable conditions, when the bile-ducts are patent, it is very advantageous to the patient to have the diseased gall-bladder removed.

Details of the technique of cholecystectomy are given, but it is curious to note that Kocher's incision, which has been abandoned by so many in favour of the right pararectal incision, is still advocated. He also states that the whole biliary apparatus must be carefully examined, for it is vital to determine if the common bile-duct is normal and to palpate its second and third parts. One is thus led to infer that if nothing is felt in the duct on palpation it contains no stone. This is, however, not correct, for all surgeons have experience of cases in which stones have been found and removed by means of forceps from the duct when nothing could be felt by external palpation. Removal from the cystic duct end is strongly advocated and stress is laid upon the important point that the duct must not be divided until the hepatic and common ducts are exposed.

A. J. W.

Renshaw, K. Malignant neoplasms of the extrahepatic biliary ducts. *Ann. Surg.*, 1922, **76**, 205.

Cancer of the biliary ducts was first recognized in the middle of the nineteenth century. The first case of cancer of the common duct was reported by Durand-Fardel in 1840, and the first of cancer of the ampulla by McNeal in 1835. Since that time but few cases have been reported, although Rolleston has collected a series of eighty-three. Of 511 operations upon the gall-bladder at the Mayo Clinic previous to 1903 there were six cases in which the growth was believed to be primary in the ducts. From 1907 to 1921 there were twenty cases at the same clinic which were confirmed by pathological examination. As a general rule the carcinoma is of the columnar cell type, although it may be spheroidal celled or mixed. Occasionally, as a result of metaplasia, a squamous-celled carcinoma may be seen as in the case of the gall-bladder. There is no reference to sarcoma in the literature. It is difficult, if not impossible, to determine the origin of tumours in the region of the papilla, since they may arise from the intestinal, pancreatic, or biliary tracts.

In the biliary tract the tumour is frequently situated in the common duct or at the junction of the common and cystic ducts, and relatively rarely in other ducts. The growth is usually confined to the walls of the ducts, and either projects internally, forming a stricture, or spreads along the tube diffusely. In any case obstruction is caused sooner or later. Metastasis seldom occurs, apparently in only about 20 per cent. of the cases.

Dilatation of the ducts above the growth is common. Dilatation of the gall-bladder will depend upon the site of the tumour. Occasionally carcinoma may arise upon a papilloma. Most of the previous reports show that there was not so close a relationship to calculi with carcinoma of the duct as there is with carcinoma of the gall-bladder, the reported frequency varying from 15–30 per cent., which is in marked contrast to carcinoma of the gall-bladder, where stones are present in 70 per cent. The previous reports also show that the condition was more common in males and was generally found between the ages of fifty and seventy.

The most constant symptom was jaundice, but not infrequently dyspeptic symptoms or attacks of colicky pain, suggesting the impaction of stone, were reported.

Operations have consisted in palliative measures, designed to make a short circuit between the dilated ducts and the intestinal canal, or in radical operations, consisting of the removal of the involved parts with re-establishment of the biliary continuity. The different methods of performing such operations are fully discussed.

It is interesting to note that the author quotes W. J. Mayo as having found an anastomosis between the gall-bladder and colon as satisfactory as an anastomosis with any other part of the intestinal canal. He also shows that the junction with the stomach is not associated with any ill effects by the passage of bile into this viscus. He then goes on to review a series of cases, twenty in all, which were found at the Mayo Clinic from Jan. 1907 to Jan. 1921, and a list of very good illustrations are given.

The common duct was found to be most commonly involved, this being the primary site in twelve cases. In four the growth was found at the junction of the common and cystic ducts. Of the twenty patients, eighteen were operated upon; palliative operations being performed in eleven; radical operations in four; and explorations in three. Stones were found in eight cases and stony material in two. Thirteen of the patients were males and seven females. The average duration of obstructive symptoms was five months, the longest fourteen months, and the shortest one month. Eleven of the patients gave a history of gall-bladder disease preceding the onset of obstructive symptoms. Loss of weight was a marked characteristic. All of the twenty cases were jaundiced.

The diagnosis was as difficult, if not more difficult, than that of carcinoma of the gall-bladder. Usually the chief symptoms are those of a preceding gall-bladder disease, with an insidious or sudden development of obstructive jaundice.

The operative mortality of the series was 33·3 per cent. and the average post-operative length of life in most of the patients was a little more than five months, one patient living fifteen months and another a little more than three years.

Full notes, with a description of the operations, are given for the twenty cases. A. J. W.

Lindsay, E. C. A case of multiple pancreatic calculi. *Lancet*, 1922, ii, 612.

But few cases of pancreatic calculi have been reported, and the majority of these have been accidentally discovered post-mortem. Lindsay gives in detail a case of a man, aged 29, who for 15 years had suffered with attacks of colicky pain in the epigastrium. The pain was worse about a quarter of an hour after food and had occasionally wakened him at night. For two years the pain had been more severe and there had been continuous wasting. Nothing could be felt on examination. The test meal showed free HCl 0·05 and a total acidity of 40. A film taken obliquely across the abdomen revealed the presence of shadows which were behind the stomach. At operation the stomach, duodenum, and gall-bladder were normal. A hard mass was felt in the position of the pancreas which on gentle pressure produced a sensation of grating. Approach was gained through the gastrohepatic omentum and an incision made into the pancreas over the most prominent mass. A quantity of pancreatic fluid containing small calculi escaped. The duct was opened up and stones removed from the whole length. Six large stones were removed, the largest being situated at the opening of the duct into the duodenum. The ducts were dilated throughout and the gland tissues relatively thin. A tube was inserted into the duct, which was then resutured. The patient made an uninterrupted recovery, the tube being removed on the sixth day and there being no further leakage.

The stones on analysis were found to consist of a calcium carbonate with a very small mixture of oxalate. A. J. W.

Banting, F. G., Best, C. H., Collip, J. B., Campbell, W. R., and **Fletcher, A. A. Pancreatic extracts in the treatment of diabetes mellitus.** *Can. M. Ass. J.*, 1922, **12,** 141.

Very valuable practical work has been done by these authors on the preparation and effects of pancreatic extracts. Since 1889, when von Mering and Minkowski produced fatal diabetes by removal of a dog's pancreas, endeavours have been made to control diabetes by feeding with pancreas or pancreatic extracts. Minkowski, Sandmeyer, and Pfluger found that feeding with pancreas was followed by negative or even harmful results. Later, Murlin, Kleiner, and Paulesco have tried the effects of aqueous extracts of the pancreas, given intravenously to depancreatized animals, and have found transitory reduction in the percentage of blood-sugar. Rennie and Fraser made use of the fact that in teleosteal fishes the islet tissue is separated from the rest of the pancreas; the administration of this islet tissue had no beneficial influence; nor was Scott able to obtain any value by the use of alcoholic extracts. Allen, and the majority of recent writers, have stated that pancreatic extracts have no clinical value whatever. The present writers have reinvestigated the problem and their results are given in the present paper.

They believe that the previous results were negative because the internal secretion, acting on the carbohydrate metabolism, was destroyed by the digestive enzymes, and therefore they attempted to eliminate these enzymes. In their first experiments this was done by taking advantage of the fact that the acinous tissue, but not the insular tissue, of the pancreas degenerates in 7 to 10 weeks after ligation of the ducts. They found that the extract made from such a pancreas, when injected intravenously into diabetic dogs, invariably caused a marked reduction in the blood-sugar and in the amount of sugar excreted in the urine. It also enabled a diabetic dog to retain a much higher percentage of sugar. Extracts of liver and spleen had no such effects. Moreover, this effect was destroyed by boiling the pancreatic juice in neutral or acid solution, or by incubating it for two hours.

In later experiments they made use of the fact that the pancreas of foetal calves of under five months' development does not contain proteolytic enzymes. By extracting such foetal pancreatic tissue a highly potent and readily procurable preparation was obtained. This was a much more practical method, and it demonstrated the principle that the extent is essentially the same from whatever animal it is prepared. A method (which is not described) was finally evolved by which an active extract, which would retain its potency for at least one month, could be obtained from normal adult ox pancreas. Daily injections of pancreatic extract, either of foetal calf or of adult beef, had most remarkable effects on dogs with experimental diabetes. Since this time they have successfully prepared potent extracts suitable to the human diabetic subject. The detailed reports of the methods of preparing such an extract will be published at an early date, but they now report the results of such applications in human diabetics.

The patients were placed on a constant diet for a week before the extracts were administered and the effects observed, the blood-sugar, the urine-sugar, the acetone bodies, and the respiratory quotient being all tested. Up to date, seven cases have been investigated, and it is evident that definite results can be obtained by administration of the extract. A fall in blood-sugar occurs, and in two cases a rise in the respiratory quotient, indicating carbohydrate utilization, occurred more or less coincidently with the attainment of a normal blood-sugar level. Patients report a complete relief from the subjective symptoms of the disease. The sugar excretion shows marked decrease, or, if dosage be adequate, disappears. Ketonuria is abolished. These results, taken together, have been such as to leave no doubt that in these extracts we have a therapeutic measure of unquestionable value in the treatment of this disease in man, but without careful control severe toxic reactions may be encountered.

A detailed report of one of the cases is given as an illustration.

A. J. W.

Osman, A. A. Splenic anaemia and chronic splenomegaly. *Guy's Hosp. Reports*, 1922, **72**, 19.

A full account is given of the development of the knowledge of splenic anaemia. Attention was first directed to the condition by Banti's paper in 1883, but, as time went on, further knowledge of the aetiology, histology, and clinical symptoms withdrew from the wide group certain definite conditions, namely Gaucher's disease, acholuric jaundice, splenomegalies of syphilis, tuberculosis, malaria, kala-azar, and von Jaksch's anaemia. There still remain many cases for which no cause has yet been found and for which, therefore, the term splenic anaemia is still applicable.

In the past twenty years about forty cases were admitted to Guy's Hospital diagnosed as splenic anaemia. Of these, only those who could be traced, or on whom post-mortems were performed, are reported, with an addition of a few in whom the diagnosis seemed fairly certain. In the present paper no attempt has been made to distinguish between splenic anaemia and Banti's disease, but it is stated that all cases of splenic anaemia, however prolonged, do not necessarily develop into Banti's third stage with cirrhosis and ascites. The onset is usually insidious, and, when acute, it is probable that only an acute exacerbation has occurred in a disease already present for some considerable time. It usually runs a prolonged course. Three cases are quoted in the series which persisted for twelve, sixteen, and twenty-four years respectively after the onset of severe symptoms; nor do they all necessarily proceed to a fatal termination, even if left untreated, and the subsequent history of four cases suggests that sometimes the disease may be a self-limited process.

No age is exempt. In early childhood it may be difficult to distinguish splenic anaemia from von Jaksch's disease owing to the fact that a normal infant's blood contains a relatively high number of white cells.

The symptoms may be divided into two groups: (1) Those consequent upon the anaemia, such as increasing pallor, breathlessness, palpitations, and lassitude. (2) Those resulting from lesions of the spleen and liver systems, such as dragging pains in the abdomen, gastric and other haemorrhages, and ascites. The most important and dangerous symptom is haematemesis. It may be the first symptom, is usually recurrent, and may be extremely severe. The source of this haemorrhage is not always apparent *post mortem*.

The spleen is moderately enlarged, the largest in the series weighing 2,286 gm. It usually retains its normal form, but the capsule is somewhat thickened and frequently shows patches of perisplenitis. Microscopically, the essential feature is the great increase of fibrous tissue. Endothelial proliferation appears to be absent except in one doubtful case. Phagocytosis of red cells is only occasionally seen. Haemorrhages and infarcts are of frequent occurrence. Cirrhosis is generally present, although it may be slight. Thrombosis of the portal and splenic veins was found in five cases. The absence of any enlargement or hypertrophy of the lymph glands is a remarkably constant feature. Varicose veins at the cardiac end of the stomach and oesophagus were found in only two cases, one of which alone had haematemesis.

It is possible that some of the cases may have been syphilitic, for it has been shown that a syphilitic splenic anaemia reacts very satisfactorily to splenectomy.

In the treatment stress is laid upon the importance of removing any possible focal infection, and if, after a reasonable time, no improvement follows, splenectomy should be considered. If a positive Wassermann reaction be obtained, antisyphilitic remedies should be given, but the treatment should not be prolonged if there is no improvement, for even here operative treatment offers the best hope of a cure. In the majority of the cases removal of the spleen is the only possible method of treatment. In the present series the operative mortality was exceedingly high, but in most of them operation was attempted as a last resort, for of seven cases under the age of twenty-five, who were treated by splenectomy, five made a complete recovery. The presence of definite cirrhosis with well-marked ascites and severe anaemia is not a contra-indication to operation, especially if an intravenous transfusion be given. Two cases are alive and well six and six and a half years after splenectomy, and three cases, two, five, and eighteen months respectively.

X-ray applications were tried in several cases but without success, with one exception. This case had X-ray applications over the spleen, and is now, sixteen years later, a comparatively healthy woman.

The value of blood transfusion can hardly be over-estimated, both to overcome the anaemia sufficiently to allow an operation and to resuscitate the patient during an extensive and formidable operation.

Detailed histories of some of the cases follows, together with a table of twenty-six cases. A. J. W.

Rolando, S. Contributo alla conoscenza del rene policistico bilaterale. [**Contribution to the question of bilateral polycystic kidneys.**] *Policlin.*, 1922, **30**, Sez. Chir., 462.

The author has studied six cases of bilateral polycystic disease of the kidney. He reviews Virchow's theory of chronic interstitial inflammation; the theory that the affection is a multilocular adenocystoma; and the congenital theory which attributes the condition to an imperfect fusion or adaptation of the two distinct germ-elements, excretory and secretory, mentioning Forssmann's study of a case in a new-born infant in which he found the obstruction in the collecting canaliculi. The author in his own case noted particularly the epithelium-covered intracystic papillae and endotubular epithelial proliferation. In the solid septa between the cysts he found normal renal tissue with zones of complete sclerosis and zones of small-celled infiltration, but these he regards, with Busse, as germinative centres of foetal origin, similar to those normally present in the embryo. He regards the co-existence of cystic disease of the liver as evidence in favour of congenital rather than neoplastic origin.

All the cases showed cachexia or metabolic defect, but, contrary to the experience of Poussin, the urine, except just at the end, was normal in quantity, specific gravity, reaction, and percentage of urea. A very small quantity of albumin and scarce granular casts were all he found before the final failure. In his own cases the urine from the two kidneys was almost always the same, but in one case, where the impalpable kidney was thought to be normal, examination of its urine revealed grave deficiency. He attributes the failure, noted by Poussin, of the 'healthy' kidney to hypertrophy as the affected one fails of its function, to the fact that though the degree may be less or the stage less advanced, the affection is always bilateral.

Haematuria is a feature of one-third of the cases; whilst generally trifling, it may be severe or fatal. Symptoms may be entirely negative. No tumour may be palpable, but of cases in which one kidney is felt enlarged, if opportunity occurs for verification, the second organ is almost always found in a like condition. The tumour may obstruct the ascending or descending colon, and in a case of Glaser's death resulted from a septic angiocholitis due to compression of the common duct by the tumour.

In diagnosis the author draws particular attention to the difficulty of palpating the left kidney, which enlarges upward, pushing up or even passing through the diaphragm and pulling with it the stomach, spleen, and splenic flexure of the colon. As a result, the lung resonance on the left side does not descend below the eighth or even seventh rib posteriorly; and, moreover, the radiographic examination shows the diaphragm raised far above the normal on the left side.

Surgical treatment, unless the second kidney can be proved competent, should be severely inactive. E. R. C.

Braasch, Wm. F., and **Scholl, A. J. Pathological complications with duplication of the renal pelvis and ureter (double kidney).** *Surg. Gynec. & Obst.*, 1922, **35**, 401–17.

One hundred and forty-four cases of duplication of the renal pelvis and ureter were observed in the Mayo Clinic during the past fourteen years. In 94 per cent. of cases the condition was unilateral.

The double kidney is usually larger than normal. A groove on the surface often indicates the boundaries of the two segments, the upper being usually the smaller, but the cellular structure often appears continuous when examined microscopically. There may be two quite distinct ureters, each draining a separate pelvis, and in this case the orifices are commonly situated close together in the normal position in the trigone: more often the ureters fuse in the lower part of their course, and in these cases the cystoscopic appearances are quite normal and the condition can only be diagnosed by pyelography: by this method both ureters and pelvis can be outlined, for it is found that, even when the end of the ureteric catheter lies in one pelvis, some of the opaque fluid usually flows back alongside the instrument and regurgitates into the second branch of the ureter and fills its pelvis. Even if this does not occur, when pyelography reveals a small pelvis lying higher than normal, then the possibility of reduplication of the pelvis and ureter should be considered.

One branch of a double ureter may end ectopically: in this series, aberrant ureters opened in the urethra in two cases, and once into the vagina. Cases have been described of ureters discharging into the seminal vesicles and into the ejaculatory ducts. Such an ectopic termination of the ureter gives evidence of its existence by urinary incontinence. Indigo-carmine injections may be of use in locating the orifice.

Of all the cases, 37·5 per cent. were suffering from pathological complications, the commonest being hydronephrosis, usually of only one segment of the kidney: another complication is atrophic pyelonephritis.

When treatment becomes necessary, nephrectomy is best, though sometimes heminephrectomy has been successfully employed. R. O. W.

Blair Bell, W. Blood transfusion. *Lancet*, 1922, ii, 501–2.

Blair Bell describes a new technique for citrate transfusion. The main point is that the citrate is added as early as possible, and this is effected by running it into the receiving canula just beyond its point of entry into the vein. The speed at which the citrate is delivered is governed by the height above the bed of the vessel containing it as well as by attention to the calibre of the delivering tube. The blood is collected already citrated into a container from which it can be transfused into the recipient. G. W.

Neuhof, H., and **Hirshfeld, S. The intramuscular administration of sodium citrate. A new method for the control of bleeding.** *Ann. Surg.*, 1922, **76**, 1–8.

In 1915, soon after the clinical application to blood transfusion of the anticoagulating action of sodium citrate, the seemingly paradoxical observation was made that the presence of citrate in the circulation of the recipient, far from lengthening the coagulation time of his blood, produced a transient shortening of it. In 1919 the writers performed a series of experiments on dogs, obtaining the following results from the intravenous injection of sodium citrate solutions: (1) the coagulation time was decreased within a few minutes, the effect sometimes being sustained for one or two days. (2) The colour of venous blood was altered to that of arterial blood. (3) The lethal dose depended even more upon the rate of introduction than on the amount of the drug and was characterized by a condition of suspended coagulation (incoagulability of the blood). It is this phenomenon which has led to the use of citrate in the operation of transfusion of blood.

In the human being, Weil had reported, in 1915, that a dose of 5 gm. of a 20 per cent. solution of citrate had reduced the coagulation time by one-half, but no details were given and no other investigators had tried any but minute doses. Neuhof and Hirshfeld therefore administered citrate to almost every surgical case admitted to their service for a period of about six months. In 200 cases of intravenous injection no untoward results occurred when the injection was given slowly and intermittently, but from experiments on animals, and from a fatal result occurring in the hands of another observer, the method was felt to be dangerous. Subcutaneous injection caused much pain and infiltration, so that the intramuscular route was finally adopted, with the following technique:

The dose for adults is 9 gm. (30 c.cm. of a 30 per. cent. solution). The citrate is dissolved in distilled water, filtered if necessary, and then sterilized in an autoclave. Two needles are inserted into the gluteal muscles, one on either side; 3 or 4 c.cm. of 1 per cent. novocaine is introduced through each needle, and after a lapse of three or four minutes 15 c.cm. of citrate solution is injected into each buttock. The pain is usually transient and there is no late infiltration. The tingling sensations, giddiness, nausea and other effects of intravenous injection of citrate are not seen with the intramuscular method. There is no alteration of the blood-pressure and no evidence whatever can be found of any toxic effect on the kidneys, even when the patient is a subject of chronic nephritis.

Within an hour the coagulation time is reduced to between two and three minutes. It remains at this level for from one to three hours, usually returning to normal within 48 hours. The same result is obtained in cases of jaundice with slow coagulation, but not in haemophilia or purpura. No changes in the C or CO_2 content of the blood have been found which would account for its altered colour. The clot formed after an injection of citrate appears to be as tough and solid as any other. In none of the patients was there any evidence of intravascular thrombosis or of embolism. In a very few patients no reduction of coagulation time was produced by the injection. Attempts to prolong the action by repeated doses showed that the effect could not be maintained for more than 4 or 5 days.

The nature of the reaction is said by Baehr and Rosenthal to be a destruction of the blood platelets with the consequent liberation of an excessive amount of a substance promoting coagulation. The sole contraindication to the use of citrate is the presence of such a disease as haemophilia or purpura in which the blood platelets are already deficient.

Apart from laboratory tests, the clinical results in a variety of cases demonstrated the potentialities of the method. It is indicated, for example, in haematemesis and haemoptysis, in the bleeding from areas such as the prostatic bed left bare by operation, and in all cases where, from jaundice or from the nature of the operation, excessive oozing is anticipated.

The results obtained by Neuhof and Hirshfeld go far to substantiate the claims they make in this interesting and valuable paper. The real crux of the matter would appear to be its bearing on those cases which exhibit a tendency to thrombosis after operation. Such cases cannot always be recognized or even suspected beforehand. Besides those that terminate fatally there are no doubt many ‘ borderland ’ cases, and the use of citrate in such a patient might be enough to turn the scale. C. C. E.

Cary, Eugene. The results of alkalinization of operative cases. *Surg. Gynec. & Obst.*, 1921, **33**, 381–5.

This article may be selected as a type of many advocating the free exhibition of alkalis as a routine procedure before and after major operations. Twenty cases chosen for observation were compared with seventeen control cases which had undergone similar operations—hysterectomy, uterine suspension, &c. On the two days preceding operation the former group were given half a drachm of sodium bicarbonate by mouth before meals and half an ounce by enema once each day. They were also given half an ounce of glucose in the enema and were encouraged to take plenty of fluids. (Others recommend pushing the bicarbonate until the urine is alkaline). Twice in the first twenty-four hours after operation they were given an enema containing two ounces of bicarbonate and two and a half drachms of glucose. In the cases so treated there was found to be less vomiting, less abdominal distension, and less frequent need of catheterization.

It is clear, both on theoretical and on clinical grounds, that where a condition of acidosis exists before operation, or where such a condition is feared because of malnutrition, glycosuria, &c., the use of alkalis is indicated. In well nourished and otherwise normal patients, however, neither the results published in this paper nor those in many similar contributions prove that the advantages claimed for alkalinization are due to anything more than the free imbibition of fluids and the supply to the patient of an easily assimilable carbohydrate both before and after operation. C. C. E.

Chiari, O. M., u. **Gamper, E.** Über das Verhalten der galvanischen Erregbarkeit der motorischen Nerven nach parenteraler Einverleibung artfremden Serums. [**On the behaviour of the galvanic excitability of the motor nerves after injection of foreign serums.**] *Deutsche Ztschr. f. Chir.*, 1922, **172**, 265.

Chiari describes three cases in which, in addition to the usual symptoms of serum disease, he noticed cramp-like spasms of the skeletal muscles after the subcutaneous injection of a prophylactic dose of antitetanic serum. The most striking feature was the trismus, so that it might be thought that the patients were really suffering from mild attacks of tetanus.

In order to investigate this point, he tested, in other cases in which a prophylactic dose of A. T. S. had been given, the galvanic excitability of the motor nerves and also their mechanical excitability, more especially that of the facial nerve, as shown by the presence of Chvostek's phenomenon.

He gives results in five cases, showing that the galvanic excitability of the radial, median, ulnar, and facial nerves was increased either on the first or second day after the injection and that this was frequently associated with Chvostek's phenomenon. This increased excitability disappeared more gradually than it arose and was lost in nine to twelve days, while a second injection of serum did not produce such a marked reaction. Two further cases in which the early changes were more closely observed suggested that there might be an initial decreased excitability to galvanism.

He refers to the resemblance to tetany, but admits that trismus is not a characteristic feature of that condition, although he mentions a case, following an operation for goitre, in which there was trismus in addition to the other symptoms. He suggests that the rheumatic pains which are recognized as a feature of serum illness may be due to the painful contraction of the skeletal muscles.

The deterioration in the general condition of a case of tetanus, which is sometimes noticed at the commencement of serum therapy may possibly be explained by the increased excitability of the nervous system produced by the A. T. S.

These observations have been made solely on clinical material and only with antitetanic serum, so that the question as to whether the results, if confirmed, can be transferred to animals and to the other sera, i.e. whether they are really anaphylactic phenomena requires further investigation. G. E. O. W.

Berti, G. Sopra due nuove specie di miceti del corpo umano. [**On two new species of Mycetae in the human body.**] *Policlin.*, 1922, **30**, Sez. Chir., 484.

In a case of mycosis in a peasant girl who habitually worked in the fields with bare feet and legs, the author isolated two new hyphomycetae, new, that is to say as regards human pathology. The lesion was a small nodular granuloma in the middle third of the leg; it formed slowly, was excised, and the wound healed by first intention. The histology showed nothing exceptional save the conidia. Intraperitoneal injection into a guinea-pig gave negative results, but by subcutaneous inoculation nodules were produced having the same histological structure as those of the original lesion, and from them the two myceti were recovered. The forms were identified and named by Prof. Pallacci of the Cryptogamic Laboratory of the University of Pavia. Their descriptions are as follows:—

Penicillium burcii n. sp. Coloniis in agaro cum glucosio cultis albis, floccosis, dein griseo-avellaneis; hyphis sterilibus ramulosis, hyalinis, septatis, repentibus vel adscendentibus, 6–7 μ diam.; conidiophoris erectis, simplicibus, septatis, hyalinis 50–110 μ longis, sursum paucos ramulos gerentibus. Ramulis in catenulas conidiorum abeuntibus; conidiis globosis, rariter elipsoides, levibus, pallide fuligineis, 4–5 μ diam.

Acremoniella bertii n. sp.—Coloniis in agaro cum glucosio cultis; hyphis sterilibus repentibus, ramosis, septatis, hyalinis, sparsis, 4–5 μ diam.; conidiophoris erectis vel curvatis, non cuspidatis hyalinis, 15–25 μ longis; conidiis globosis, continuis, 6–7 μ diam. fuscis.

Cultures of each of these moulds, on hypodermic inoculation produced the characteristic lesion in guinea-pigs, without notable difference from that produced by their conjoint action. E. R. C.

NEUROLOGY

Thalhimer, W. Epidemic (lethargic) encephalitis. Second communication. *Arch. Neurol. & Psych.*, 1922, **8**, 286.

The author has carried out a fresh set of cultural and experimental studies with results entirely confirmatory of those obtained in previous investigations to which reference has already been made (*Medical Science*, 1922, **6**, 396). C. D. F.

Goldstein, K. Über anatomische Veränderungen (Atrophie der Substantia nigra) bei post-encephalitischem Parkinsonismus. [**On the anatomical lesions (atrophy of substantia nigra) in post-encephalitic Parkinsonism.**] *Ztschr. f. d. ges. Neurol. u. Psych.*, 1922, **76**, 627.

In subacute and chronic cases of lethargic encephalitis, which have been characterized by a parkinsonian syndrome, with or without tremor, the substantia nigra is remarkably atrophic. The atrophy is due to the degeneration and total disappearance of a great number of nerve-cells, the melanin granules of which are in part collected by macrophages and proliferated neuroglia cells, in part eliminated through the blood-stream. C. D. F.

Horrax, G. A consideration of the dermal versus the epidermal cholesteatomas having their attachment in the cerebral envelopes. *Arch. Neurol. & Psych.*, 1922, **8**, 265.

Conclusions: There is a group of rare intracranial tumours which represent foetal epiblastic inclusions, sometimes of the epidermal layer alone, sometimes including also the dermal layer. These tumours may or may not contain hair and other tissue elements according to the depth of the cell-layer represented in the inclusion. It is convenient to group all these tumours under the term cholesteatomas, either hair-containing or non-hair-containing. Three examples of the hair-containing variety (intracranial dermoids) are described. Two of them were removed by operation, with apparent success in one case. C. D. F.

Eskuchen, K. Der Liquor cerebrospinalis bei Encephalitis epidemica. [**The cerebrospinal fluid in epidemic encephalitis.**] *Ztschr. f. d. ges. Neurol. u. Psych.*, 1922, **76**, 568.

The author takes into account the results obtained by personal investigations and the conclusions reached by other authors. In his opinion the 'fluid syndrome'—pleocytosis, increase in globulins and sugar, and colloidal gold reaction of the luetic type—is, in the main, characteristic of lethargic encephalitis. C. D. F.

Raphael, Th., and **Parsons, J. P. Metabolism studies in dementia praecox and manic-depressive insanity. Second paper.** *Arch. Neurol. & Psych.*, 1922, **8**, 172.

In normal conditions the blood-sugar rise following the intramuscular injection of 1 mgm. of epinephrin is maximal in from 30 minutes to 1 hour, with subsidence in 3½ hours. The point of minimal glycaemia is definitely below the initial fasting level, after which there is a return to approximately this level. In cases of dementia praecox and manic-depressive insanity the point of minimal glycaemia is lower than that found in normal subjects, and there is only a slight or no return to the fasting level.

C. D. F.

Weston, P. G., and **Howard, M. Q. The determination of sodium, potassium, calcium, and magnesium in the blood and spinal fluid of patients suffering from manic-depressive insanity.** *Arch. Neurol. & Psych.*, 1922, **8**, 179.

In order to determine whether the manic and depressed phases of manic-depressive insanity are associated with an alteration of the normal balance of Na, K, Ca, and Mg in the blood and cerebrospinal fluid, analyses were made of these two fluids in 17 cases of mania and in 10 of depression. The average of these elements was practically the same in both states and the individual variations from the average were small. With respect to Ca no variation from the normal in either blood or spinal fluid was found. As regards the other three elements no definite conclusions could be reached in the absence of any long series of analyses of normal blood and spinal fluid. C. D. F.

Lorenz, W. F. Sugar tolerance in dementia praecox and other mental disorders. *Arch. Neurol. & Psych.*, 1922, **8**, 184.

Except in active catatonia, certain cases of simple deteriorating dementia praecox, and several cases in which an evident emotional upset existed at the time of the test, the blood-sugar concentration of patients affected with various mental disorders was found to be practically normal when the test was carried out while the patients were fasting. The response of these patients to sugar feeding was likewise within normal range. Active cases of catatonic dementia praecox responded to glucose feeding with a hyperglycaemia similar to that obtained in hyperthyroidism, while patients affected by the simple deteriorating form responded in a manner similar to that found in dyspituitarism. During the depressive phase of manic-depressive insanity the sugar-test curve is higher than in normal conditions. C. D. F.

Volpino, G., e Racchiusa, S. Influenza ed encefalite sperimentale. [**Influenza and experimental encephalitis.**] *Ann. d'ig.*, 1922, **32**, 721.

A form of subacute encephalitis was obtained in rabbits by subdural inoculations of the glycerinated expectoration of three typical cases of influenza. The fresh expectoration was collected in sterilized bottles, washed with water in order to eliminate the salivary keratogenous virus of Levaditi, and then kept in pure glycerol from 5 to 15 days. Control experiments were made with the expectoration from apparently healthy subjects and from cases of lung tuberculosis and pneumonia. After a period of incubation of 3 to 5 days the inoculated animals became affected with a disease lasting 10 days and characterized by symptoms similar to those of lethargic encephalitis. The histological examination of the brains of the affected rabbits revealed the existence of an inflammatory process characterized by nerve-cell degeneration associated with neuronophagia, parenchymatous and perivascular infiltrations chiefly consisting of 'mononuclear cells' of the lymphocytic type. Polymorphonuclear leucocytes were not seen. In the cytoplasm of a considerable number of nerve-cells large eosinophil bodies were found, which, judging from the coloured plate illustrating this paper, have a striking resemblance with Lipschütz's intranuclear α-, β-, and zoster-bodies (*Medical Science*, 1922, **6**, 313). The bacteriological investigation of the brains of the affected rabbits was attended by negative results. Control animals either died of acute infections or remained apparently healthy. The glycerinated virus used by the authors is neither filter-passing, nor keratogenous, nor transmissible in series to other animals.

C. D. F.

Weimann, W. Über das Vorkommen 'amyloider Substanzen' im Gehirn bei der Encephalitis epidemica. [**On the occurrence of 'amyloid substances' in the brain of a case of epidemic encephalitis.**] *Monatschr. f. Psychiatr. u. Neurol.*, 1922, **51**, 300.

The frequent occurrence of corpora amylacea in the central nervous system from cases of lethargic encephalitis has already been pointed out by Gamna, Gross, and Spiegel. In the case now described by Weimann amyloid substances were, in addition, found within nerve-cells and glia-cells. The clinical symptoms and histo-pathological lesions were those usually seen in acute and subacute cases of the malady. However, it is worth noting that the nerve-cell degeneration was very extensive. In the cerebral cortex cells of all layers were diffusely affected, and in the grey matter of the basis cerebri the degeneration had gone so far as to reduce many nerve-cells to mere 'shadows'. Various important alterations of the nuclei of nerve-cells were also noticed, while the neuroglia of all affected areas showed signs of active proliferation. The amyloid substances were observed under the various forms of: (1) corpora amylacea disseminated almost everywhere, but particularly numerous round the Sylvian aqueduct; (2) irregular amyloid clumps limited to the neighbourhood of both sensory nuclei of the trigeminus; (3) amyloid bodies undoubtedly situated within the nerve-cells of the same region; (4) amyloid granules situated within the neuroglia cells, particularly of those places where the amyloid clumps were most abundant. The interest of these observations lies chiefly in the fact that the presence of amyloid bodies within nerve-cells has been so far described in only three other instances by Lafora, Westphal, and

Bielschowsky. In the two cases of myoclonus epilepsy investigated by Lafora and Westphal intracellular amyloid bodies were seen in every part of the central nervous organs, while in the case of double congenital athetosis published by Bielschowsky the lesion was limited to a small number of nerve-cells of globus pallidus. C. D. F.

Tarozzi, G. (1). Sulla patogenesi delle alterazioni istologiche dei centri nervosi nella encefalite cosidetta letargica. [**On the pathogenesis of the histological lesions in the central nervous system of cases of so-called lethargic encephalitis.**] *Riv. di patol. nerv.*, 1922, **27**, 48.

Tarozzi, G. (2). Encefalite non suppurativa seguita ad erisipela da ferita traumatica del capo. [**Non-suppurative encephalitis consequent upon erysipelas from a traumatic wound of the head.**] *Riforma med.*, 1922, **38**, 841.

The author has already shown (*Medical Science*, 1922, **6**, 315) that changes of the central nervous system, similar to those seen in cases of lethargic encephalitis, may be obtained in rabbits by means of subdural inoculations of the filtered and sterile fluid of cultures of diplo-streptococci isolated from the pulmonary foci of cases of influenza. In connexion with his previous work, he now publishes some interesting drawings and the following case. A previously healthy man, who had been severely wounded in the head with a stick, developed a few days afterwards a fatal form of erysipelas of the head and forehead. In the course of the disease, fever, delirium, and stupor were noticed. The patient died fourteen days after having been wounded. The histological examination of the brain revealed the existence of a diffuse meningo-encephalitic process in every way similar to that observed in cases of lethargic encephalitis. The perivascular infiltrations consisted of cells of the ‘ lymphocytoid type ’, and were particularly abundant in the lenticular nucleus, optic thalamus, and midbrain. Polymorphonuclear leucocytes were not seen, and bacteriological investigations were attended by negative results. For these reasons, and in consideration of his previous experimental investigations, the author put forward the suggestion that lesions of the central nervous system of the type of those observed in cases of lethargic encephalitis may be due to toxins circulating with the blood-stream. The author excludes the supposition that the case now described was one of sporadic lethargic encephalitis with lesions only apparently connected with the erysipelatous infection. C. D. F.

Pette, H. Klinische und anatomische Betrachtungen über die Frage der Zusammengehörigkeit von Amyotrophie und Tabes dorsalis. [**Clinico-anatomical considerations on the relationship of amyotrophy and tabes dorsalis.**] *Ztschr. f. d. ges. Neurol. u. Psych.*, 1922, **77**, 275.

The view originally sustained by Déjerine, Westphal, Oppenheim, and others, that the occurrence of muscular atrophy in tabes was due to a peripheral nerve lesion has given place in more recent writings to the conclusion that the ventral horn cells are the seat of the lesion, and this indeed was Charcot's observation many years ago. The author supports the latter view and records in detail, clinically and pathologically, a personally-observed case of tabes with amyotrophy. The patient was a woman of 52, with a twelve years' history of tabetic symptoms, who eighteen months before death developed muscular wasting. This made its first appearance in the left thenar eminence, but spread rapidly, involving the entire left arm and shoulder and left side of the neck, then the thoracic and abdominal muscles, and finally those of the legs. In other respects, the case was of the ordinary type. Fibrillation was an early but transient phenomenon in the affected muscles. The electrical excitability diminished progressively, and the reaction of degeneration occurred transiently in a few muscles only. Microscopical examination of the nervous system and muscles gave the following results. In the muscles, areas of normal muscle fibrils alternated with grossly altered areas. In the latter the fibrils were of unequal size, some shrunken and others swollen in appearance. The sarcolemmal nuclei were increased and striation lost. In the peripheral nerves supplying the wasted muscles, Marchi degeneration was very pronounced and Weigert preparations showed extensive myelin sheath destruction. The brain presented no abnormality. Weigert preparations of the cord showed the typical tabetic changes in the posterior columns, with some infiltration of the meninges. In addition, the grey matter of the ventral horns was profoundly altered. At all levels the cells were shrunken and diminished in number, and the grey matter was infiltrated by small lymphocytes and plasma cells. The vessels showed no definite thickening of their walls and no proliferation. The glia was markedly proliferated. Throughout the entire cord, but especially in the cervical and upper thoracic segments, the majority of the large ventral horn cells had disappeared. Those remaining showed chronic degenerative changes. A few normal cells were still to be seen. Similar, but less intense, pathological changes were present in the cells of Clarke's column and those of the dorsal horns. The dorsal root ganglion cells showed the changes usually found in tabes, and the radicular nerves were surrounded by fresh granulation tissue, as described by Richter (cf. *Medical Science*, 1921, **4**, 547), with the addition, contrary to Richter's findings, of small lymphocytes and plasma cells.

Pette reviews the history of the subject and attributes to Schaffer the merit of having established the central origin of tabetic amyotrophy on a sound basis. From his summary of the clinical features of reported cases it appears that an onset in the small hand-muscles with subsequent spread up the limb is the usual mode of onset (Aran-Duchenne type), and is followed by involvement of the chest and abdominal and lower limb muscles successively. In some instances, however, instead of this steady spread from a single focus, various foci anatomically remote make their appearance. Fibrillation is commonly an early and transient symptom, and the characteristic electrical change, as in his own case, is a steady diminution of excitability, that is, a quantitative rather than a qualitative change. This he attributes to the persistence of normal nerve-fibres in the affected nerves, stimulation of which always produces contraction of normal type in a certain number of muscle-bundles. Moreover, he believes that the clinical features of the atrophy themselves indicate a central rather than a peripheral origin. In this connexion he instances the topography of the wasting which is segmental and not peripheral in type, the presence of fibrillation, and the sequence of .weakness after atrophy. Finally, the character of the electrical changes in the muscles affected points to the same conclusion. Pathological investigation shows that the muscle atrophy corresponds in distribution and intensity with the ventral horn-cell lesions. The presence of lymphocytic and plasma-cell infiltration in the affected areas of grey matter also indicates that the cell changes are primary and are not the result of an initial peripheral nerve degeneration.

In discussing the cause of the ventral horn-cell lesions, Pette refers to Lapinsky's well-known observation that section of the dorsal roots proximal to the dorsal root ganglia leads at once to acute cell changes in the ventral horn cells of the corresponding segments. Pette doubts whether these acute traumatic changes can be correlated with the chronic progressive lesion found in tabes. If it were so, we should expect to see amyotrophy as the rule rather than as the exception in tabes. Moreover, while Lapinsky's experiment led not alone to degeneration of dorsal root collateral fibres, but also to changes in the walls of the blood-vessels and degenerative changes in the pyramidal tracts in the corresponding segments of the cord, in Pette's case the two last-named elements were absent. Nor can the posterior column degeneration be correlated with the cell lesion, for the two did not correspond accurately in topography or intensity. Also, when, as may be the case, muscles supplied by cranial nerves are involved, this explanation cannot hold. Pette inclines to the view that just as in general paralysis we have a lesion of the cells of the brain associated with infiltration by lymphocytes and plasma cells, so a lesion of a similar nature may develop in the grey matter of the cord producing a syphilitic amyotrophy. The isolated occurrence of such an amyotrophy is well recognized, and there is no inherent reason why we should not see it combined with tabes from time to time, just as the lesions of general paralysis may be. Thus tabes + amyotrophy would be strictly analogous with tabes + general paralysis. This, indeed, is the conclusion at which Pette arrives, while admitting that in the present state of knowledge it remains but an hypothesis. F. M. R. W.

Charles, J. R. Three cases of manganese poisoning. *J. Neurol. & Psychopathol.*, 1922, **3**, 262.

The commonly accepted clinical picture diagnostic of manganese poisoning is given by the author as including among its component symptoms emotional disturbances with uncontrollable laughter or weeping, mental languor, muscular rigidity and tremor, and the general appearance of Parkinson's disease. There are no signs of pyramidal system disease. Commercially, manganese is used in making chlorine gas, paint, varnish, enamel, and linoleum, for the marbling of soap, and in the manufacture of steel.

Case 1 was a manganese worker, and shortly after taking up the work he began to grow weak and voiceless. His gait was altered, on the level he shuffled, but going up hill he had to walk on tip-toe. He gave up the work after seven months, two years before coming under observation, but had not changed in condition during the interval. Examination revealed no visceral disease. He spoke in a whisper, and his face was immobile and expressionless. Otherwise, the cranial nerves were normal. There was general muscular weakness, but no inco-ordination. The tone of the upper limbs was normal, but the legs were rigid and the gait dragging. He walked on his toes. There was a tendency to fall backwards, which, owing to muscular rigidity, he did in a statuesque fashion. The reflexes were all normal.

Case 2 was also a manganese worker (shovelled manganese ore), who had followed this occupation for three years. To a clinical picture like that described for Case 1 were added some signs of an old syphilitic myelitis.

Case 3. The patient had worked in a manganese works for several months seven years before. He had been forced to give up work with symptoms resembling those described in the two previous cases. He also suffered from rheumatic pains in the legs and with hesitant micturition. He had done no work for five years previous to coming under observation. Physical signs were as in Case 1. Examination of the blood revealed no abnormality.

The author correlates these symptoms with a lesion of the corpus striatum. F. M. R. W.

Dunlap, C. B. Recent studies on spirochetes in general paralysis. *Arch. Neurol. & Psych.*, 1922, **8**, 589.

Dunlap reviews recent work on the occurrence of spirochaetes in the brain of general paralytics, more especially the papers of Jahnel, Sioli, and Hauptmann.

Jahnel has developed a new silver impregnation method for the detection of spirochaetes in the central nervous system, which has the advantage of not staining axis cylinders. By this process the organism has been demonstrated in as high proportion as 50 per cent. in some series. Brain puncture during life and examination with the dark-ground condenser has given an even higher percentage of positive results. Spirochaetes may be observed in any part of the brain, but the most favourable situation in which to seek for them is the frontal lobes, where they occur in the middle and deep layers of the cortex. It is very exceptional to find them in the pia or in the subcortical white matter. They are most readily found in cases which have run a stormy clinical course, with convulsions, sudden paralytic and apoplectic attacks. The most favourable opportunity of all is when a patient dies in such a seizure, when the spirochaetes may be found in swarms. It is said that they survive their host, being resistant to decomposition, and that they migrate after death. The spirochaete of general paralysis probably does not belong to a special biological strain, but is the ordinary organism, modified biologically during its residence in the host. The time and manner of its entrance into the parenchyma of the nervous system remains undetermined. There seems no real justification for the differentiation of parenchymatous and meningo-vascular syphilis of the nervous system. In general paralysis it is exceptional to find the spirochaete in any other organ than the brain. Jahnel has reported its occurrence in the aorta. F. M. R. W.

Bazett, H. C., and Penfield, W. G. A study of the Sherrington decerebrate animal in the chronic as well as in the acute condition. *Brain*, 1922, **45**, 185.

All previous experiments on the 'decerebrate animal' in the sense adopted by Sherrington have been acute in the sense that the preparation survived for a few hours only. The earlier experiments of Goltz and others on dogs, in which the animal survived for months, or even for over a year, differed in that the midbrain and the greater part of the thalamus remained intact, and the animal was not rigid and retained temperature control. In other words, these animals corresponded to Magnus and de Kleijn's 'thalamus' animals, which were described in a recent number of this Journal (*Medical Science*, 1922, **7**, 109). Strictly speaking, therefore, the 'decerebrate animal' is one from which not only cerebral hemispheres but also the brain-stem down to and including the anterior portion of the midbrain have been ablated.

In these circumstances, the animal becomes spastic in extension. Bazett and Penfield, for the first time, have succeeded in keeping such experimental preparations alive for as long as three weeks, by immersing them in a bath at constant temperature in an incubator. They describe in detail the difficulties which beset them in this task, and which depend in large part on the complete loss of temperature control which these animals show.

Their observations are of great interest, both anatomically and physiologically. In the latter respect, they confirm Sherrington's observations as to the characters of decerebrate rigidity, and in the former the study of the descending degenerations in brain-stem and cord has given us much new information.

The authors express their conclusions as follows :

Chronic decerebrate preparations (cats) are found to maintain throughout their period of preservation the general characteristics described by Sherrington. The extensor rigidity is maintained with brief intermissions, indicating that it is a true 'release phenomenon'. The rigidity persists after the descending degenerations in the brain-stem and cord are complete and after complete degeneration of the cells of the red nucleus. The rigidity probably depends upon a reflex arc, the centre for which lies in the brain-stem at the plane of Deiter's nucleus. This nucleus and Gower's ventral spino-cerebellar tract never showed any evidence of degeneration in any of the preparations examined.

In the later stages there is a tendency for flexed postures to be taken up, and these may be asymmetrical. Flexion of the forepaws with extrusion of the claws was very common. The preparations show no temperature control and never shiver, though after unilateral decerebration, when this control always persists, shivering may be seen.

The essential factor in the preservation of the animals is the maintenance artificially of a normal body temperature. Apart from variations due to changes in body temperature, the respiratory rate is that normal for the cat.

Head retraction and opisthotonos occur when the rigidity is extreme, and are always associated with other 'irritative' symptoms, such as respiratory irregularities and tonic fits. All these occur in association with progressive haemorrhage beneath the tentorium and raised intracranial tension. Pseudaffective reflexes appeared within a few days of decerebration. They included movements of the head away from nocuous stimuli, movements of the forelimbs, mastication, nose-licking, and in a few instances purring and vocalization occurred.

When the plane of transection lies well forward, progression movements are seen. Acoustic reflexes are also to be observed. For two or three days after decerebration there is glycosuria. Its cessation is not caused by disappearance of glycogen.

Unilateral decerebration is followed by the development of extensor rigidity in the homolateral limbs and by rotation of the head towards the side of removal. In about three days these phenomena are constantly replaced by the development of extensor rigidity in the contralateral limbs and by rotation of the head to the crossed side. The initial head posture and rigidity the authors regard as a transient excitation phenomenon, replaced later by a permanent 'release' stage. In some unilateral cases, flexor rigidity or bilateral extensor rigidity developed. They believe that the pathway, whose interruption is responsible for the appearance of the rigidity, decussates in the midbrain.

Occasionally in bilateral as well as in unilateral decerebrations flexor rigidity was observed. It is thus possible to speak of two types of decerebrate rigidity.

The close study of this paper in the original may be recommended to neurologists, and it should serve as a useful corrective of the somewhat loose notions now current as to the features of decerebrate rigidity (cf. *Medical Science,* 1923, **7**, 398). F. M. R. W.

BACTERIOLOGY

Morrison, L. F. On the origin of alexin (complement) in guinea-pig blood. *J. Immunol.*, 1922, **7**, 435.

First of all a plea is made for the retention of the word 'alexin' as contrasted with that of 'complement'. Reasons are given based on historical grounds and also those of correctness. Then follows an investigation into the alexin content, and the nature of alexin in the blood of normal male guinea-pigs. The research is divided up into four parts, with a discussion and set of conclusions.

(i) The quantitative determination of alexin—with the time and temperature relations in clotted and defibrinated blood.

(ii) A comparison of the alexin-content of clotted blood and plasma (salted, oxalated and paraffin plasma).

(iii) The reactivation of the alexin-content of aged guinea-pig serum.

(iv) The enzymatic nature of alexin.

The following are the author's conclusions:

A far more powerful alexin, ready for immediate use is obtained by the defibrination, centrifugalization, and removal from the cells of guinea-pig blood-serum than is obtained by the usual method of allowing the blood to clot and removing the serum after it has been allowed to stand on the clot for 24 hours.

The same time and temperature relations, as have been worked out for clotted blood-serum alexin, hold true for the defibrinated blood-serum alexin-content.

The leucocytic theory of the origin of alexin, is not tenable when the data detrimental to such a theory, now available, are taken into consideration. The experimental evidence presented showing the apparent inactivity of either the red or white blood corpuscles to produce alexin, together with the fact that blood-plasma contains large amounts of alexin, offer themselves as strong arguments against such a theory.

There is a gross difference between serum inactivated by heating to 56° C. for one hour, and serum allowed to stand at room temperature until it has lost its alexin-content, in their reactibility on the addition of fresh guinea-pig serum, high in alexin-content. This is due to the adsorption of the alexin of the fresh serum by the larger molecules of the heated serum.

The reactivation of the old serum may be explained by the enzymatic nature of alexin or by assuming there are two thermolabile fractions of alexin, one being more susceptible to the detrimental effects of time and temperature than the other. Fresh guinea-pig serum allowed to stand at room temperatures for several days showed no further evidence of 'complementoids'. Further data in corroboration of the enzymatic nature of alexin were obtained. W. A. M. S.

Lundberg, E. G. On the photolability of serum complement. *J. Immunol.*, 1922, **7**, 389.

The purpose of this investigation was to discover the laws governing the destruction of complement (alexin) in normal serum by light. Inactivation of complement by other means such as heat, shaking, acids and alkalis has been quantitatively studied, but apparently photo-inactivation has been studied only qualitatively, hence this research. While the work was in progress the researches of S. C. Brooks on the same subject, but with different technique, came to the notice of the author, who compares his work with that of other workers.

The complement used was undiluted normal swine serum. For radiation there was employed a mercury-gas quartz lamp (140 volts, 4·3 amperes). The absolute light strength was never measured, but a constant range was kept between serum and lamp—except when purposely varied to change the relative light intensity. Details of the technique then follow. Serum concentration (p) is plotted against haemolysis percentage (h). Each h is divided by its corresponding p. Then the fraction h/p indicates the efficiency-value of the serum mixture in question. If n is the number of terms, the mean value $\frac{\Sigma h/p}{n}$ is found. It is not constant, but reaches a maximum value—here used as a measure of the complement strength s. The reaction constant k is calculated for each curve out of the observed values, using the formula for mono-molecular reactions $k = \log \frac{a}{a-x} \Big/ t \,.\, \log e$ where a is the original complement force, $a-x$ the remaining force after t minutes, and e is the basis of the natural logarithms. Thus the symbol k gives a measure of the observed speed of destruction.

The influence of temperature on these reactions was investigated in order to find the k values in the Van't Hoff-Arrhenius formula $k_1/k_2 = e^{\mu(T_1-T_2)/2T_1T_2}$ where T_1 and T_2 are the absolute temperatures in the two reactions running at speed k_1 and k_2, and μ is the desired temperature coefficient. Experiments were also made to see if alteration of the lamp distance really produced the effect one might expect beforehand, viz. $k \propto 1/(\text{distance})^2$. Also, the effect of dilution was investigated.

The results found were:

(i) Light-destruction was fairly well represented by the mono-molecular formula.

(ii) The rate of destruction is low, k varying from 0·019 to 0·050.

(iii) The temperature coefficient (μ) is small or none. μ does not exceed 2/1,000 to 3/1,000, which signifies an increase in k of 1·1 to 1·7 per cent. for 1° C. increase of temperature at 27° C.

(iv) Variation in lamp distance causes changes in reaction speed which do not differ essentially from inverse proportionality to the light intensity.

(v) Dilution of serum before radiating causes not only the expected decrease of complement strength but alters very irregularly its magnitude. It causes too, an increase in reaction speed, which however is not parallel to the dilution amount.

(vi) The colour of the serum changes obviously during radiation from orange to dull yellow, the opalescence increasing at the same time. This is accounted for in the colorimetry.

(vii) As regards the exactness of the measurements made with this method, the primary figures have a possible error of about ± 10 per cent. The graphically found values may be regarded as more exact. The h values are chiefly found to differ within ± 12 per cent. from the mean. The temperature variation in each experiment, being within ± 0·4° may be disregarded in consequence of the insignificant temperature influence.

W. A. M. S.

Ecker, E. E. The action of the visible spectrum on complement. *J. Infect. Dis.*, 1922, **31**, 356.

The inhibitory power of the invisible (ultra-violet) rays on complement has received extensive recognition. Most of this work has been done by direct exposure of sera to the ultra-violet rays, varying the thickness of the exposed liquids; or by dilution, ending with a simple complement titration. It appeared to the author that attempts to study the effect of the visible rays on complement and amboceptor were lacking. Hence, the present research was decided upon. The effect of the visible spectrum on complement is one of inhibition. Exposed sera do not produce haemolysis in the same unit of time as sera kept in darkness, and may even be greatly reduced in their complementary action if the exposures have been sufficiently long. Haemolysis is distinctly delayed, and if the exposures have been made for a long enough period the effect produced is lasting. Red and infra-red rays delay the activating action of the complement. At the violet end of the spectrum inhibition is marked. Dried sera are more resistant to the action of light, and only prolonged exposures are able to weaken the complement, while diluted sera are much less resistant. The decrease of complementary power after an exposure of six hours, for instance, does not continue after the radiation is terminated. The reaction, then, is not continuous. This confirms the work of Bovie and Brooks, and of Huber for exposures of rennin to ultra-violet rays. With continued exposure, however, attenuation markedly increases, as pointed out by Lundberg. The nature of light action on complement is still problematical. It appears to be a purely chemical change. Abelin and Stiner state that the action of ultra-violet light is one of molecular change and give as an example the change of the poisonous yellow phosphorus into non-poisonous red phosphorus. The action does not take place with absorption. Bovie showed that 20 per cent. of the cells protect complement from destruction, and Soret has shown that most proteins exhibit an absorption band in the ultra-violet end of the spectrum and that solutions of tyrosine exhibit this phenomenon most markedly. Only tyrosine and phenylalanin seem to show this property as shown by Kober. Whatever the nature of photosensitiveness of complement, light inhibits and destroys complement. Its action can be antagonized by the use of a member of the aromatic-amino-acid series as shown recently by McCoy, Hill and Schmidt. It remains for future work to determine the exact nature of this effect. W. A. M. S.

Ecker, E. E., and **Rees, M.** **Effect of haemorrhage on complement of blood.** *J. Infect. Dis.*, 1922, **22**, 361.

Complement has a regular curve of decrease and regeneration following a single severe haemorrhage. It is unaffected by subsequent dilution of the blood by the body fluids. The curve does not run parallel to that of any of the cellular elements circulating in the blood following haemorrhage, nor is there reason to believe that any of these cells is a factor in the regeneration of complement. The initial decrease is due to dilution of the blood, which decrease is soon overcome and restored to normal by an influx of complement from some, as yet unknown, source. Repeated haemorrhages with extreme degrees of anaemia and subsequent recovery do not alter the level of complement. W. A. M. S.

Fleming, A., and **Allison, V. D.** **Further observations on a bacteriolytic element found in tissues and secretions.** *Proc. Roy. Soc.* B, 1922, **94**, 142.

The important work of one of the authors (Fleming) was referred to in *Medical Science* (1922, **7**, 255). It was shown that 'lysozyme' existed in tissues and secretions and was lytic for various micro-organisms, but particularly for *Micrococcus lysodeikticus* discovered by the author. In the present paper the matter is carried still further, and it is shown that strains of *M. lysodeikticus* resistant to lysozyme action can be readily developed. The resistance is not specific, i. e., strains made resistant to one tissue or secretion are equally resistant to all tissues whether derived from man, the lower animals, or from vegetables, showing that the lysozyme affecting *M. lysodeikticus* is the same whatever its source. After solution of large quantities of *M. lysodeikticus* there is an increase in the lytic power of the fluid and this increase affects mainly or wholly the homologous microbe., W. B.

Rizzo, C. Considerazioni sulla reazione di Wassermann e sui metodi a precipitazione colloidale nel liquido cefalo-rachidiano dei neurosifilitici. [**On Wassermann's reaction and colloidal precipitation tests for the cerebrospinal fluid of neurosyphilitics.**] *Riv. patol. nerv.*, 1922, **27**, 1.

The following conclusions were reached: (1) The reactions obtained from the cerebrospinal fluid by colloidal precipitation tests (gold, Prussian blue, benzoin, &c.) are not specific for neurosyphilitic lesions and cannot be relied upon for the discrimination between different forms of syphilis of the central nervous system. They simply indicate the existence of an inflammatory or irritative condition of the nervous system. (2) Only a positive Wassermann reaction is a certain indication of a neurosyphilitic lesion. (3) The cerebrospinal fluids of some neurosyphilitics give a positive Wassermann reaction only if not inactivated. Whenever possible the reaction should, therefore, be carried out at the same time on the inactivated and not-inactivated fluid. (4) Fluids, the reaction of which becomes negative after inactivation, show a positive benzoin reaction before and after inactivation. (2) A Wassermann reaction, positive only by the use of a not-inactivated cerebrospinal fluid, is specific if the fluid does not coagulate or show any xanthochromia or hyperalbuminosis. (6) In general paralysis the intensity of the Wassermann reaction is approximately the same with the use of inactivated or not-inactivated fluid. (7) In cases of cerebral syphilis and of uncomplicated tabes dorsalis, thermolability of the cerebrospinal fluid is important from the diagnostic point of view and has a favourable prognostic significance. C. D. F.

Izar, G., e **Caruso, G.** (1). Sulla precipitazione e concentrazione di sostanze a funzione di anticorpi. [**On the precipitation and concentration of substances functioning as antibodies.**] *Riforma med.*, 1921, **37**, 1123.

Izar, G., e **Caruso, G.** (2). Isolamento del complesso antigene più anticorpo. [**Isolation of the complex antigen plus antibody.**] Ibid., 1922, **38**, 145.

(1) By means of additions of re-distilled water it is possible to separate from blood-serum substances which react specifically with the corresponding antigens. The quantity of specific substances (antibodies) thus precipitated varies according to the amount of re-distilled water added, but beyond a certain limit non-specific substances are also precipitated. The proportions of blood-serum and re-distilled water vary according to the kind of antibody one wishes to precipitate; in the case of haemolytic antibodies 3 or 4 volumes of water should be added to 1 of blood-serum, while agglutinating antibodies are precipitated by the addition of 30 volumes of water to 1 of serum, and substances able to fix the complement in the presence of a luetic antigen are precipitated by an addition of 5 to 7 volumes of water. The method cannot be used for the separation of precipitins.

(2) When re-distilled water is added to the complex antigen plus antibody, a precipitate is obtained which after centrifuging and washing with re-distilled water still fixes the complement. The precipitate has specific properties only if obtained from fresh and not-inactivated serum, and if the addition of water does not go beyond a certain limit. The proportions between complex and re-distilled water vary a little according to the nature of the serum. C. D. F.

Petriccioni, E. Ricerca del bacillo difterico nelle urine di malati di difterite. [**On the presence of *B. diphtheriae* in the urine from cases of diphtheria.**] *Ann. d'ig.*, 1922, **32**, 212.

B. diphtheriae was isolated from the urine of one out of twenty cases of diphtheria. Therefore the danger that the disease might be propagated through urine is very small. In the same fluid diphtheroid bacilli are frequently found which, on a superficial examination, might be confused with *B. diphtheriae*. Hence the necessity of having resort to cultural and biological tests in all dubious cases. C. D. F.

Rondoni, P. L'influenza della tossina difterica sulla innervazione respiratoria. [**Influence of diphtheric toxin on respiratory movements.**] *Arch. fisiol.*, 1922, **20**, 293.

Intravenous injections of large doses of diphtheric toxin have a noticeable though varying influence on the respiratory movements of rabbits. The injected animals show the effect of bilateral vagotomy sooner and more intensely than normal animals. C. D. F.

Rigobello, G. Comportamento del bacillo difterico e del pseudodifterico nella bile (in coltura e nell' organismo). [**Behaviour of *B. diphtheriae* and *B. pseudo-diphtheriae* in the presence of bile in cultures and in the organism.**] *Ann. d'ig.*, 1922, **32**, 208.

Bile is not a means favourable to the development of *B. diphtheriae*, either in cultures or in the organism. However, it may be usefully employed to discriminate between *B. diphtheriae* and *B. pseudodiphtheriae*.

C. D. F.

Pergola, M. Il mio metodo di ricerca del bacillo difterico nella pratica dell' accertamento diagnostico della difterite. [**My method of investigation of *B. diphtheriae* with reference to the bacteriological diagnosis of diphtheria.**] *Ann. d'ig.*, 1922, **32**, 629.

Reference has already been made to the methods proposed by the author for the cultivation and enrichment cultures of *B. diphtheriae* (*Medical Science*, 1922, **5**, 428). He has now had the opportunity of trying his methods on a relatively large scale with the following results: Culture medium B is particularly useful for the isolation of *B. diphtheriae* and medium I for the enrichment culture. Culture medium B consists of:

Normal blood-serum of ox, horse or goat . . .	50 c.cm.
0·8 per cent. solution of NaCl	50 „
2 per cent. solution of sodium tellurite (H_2TeO_3) .	1 „
Yolk of egg	1 „

The medium should be solidified by warming it for one hour at 85° or 90° C. and then poured into ordinary test-tubes or plates. Medium I has the same constitution but it should be kept fluid. This is effected by sterilizing it in a water bath at 50° to 55° C. for half an hour during three successive days. Loeffler's serum was used for comparison. *B. diphtheriae* was found in 45·80 per cent. of all cases investigated by means of the author's media, while by means of Loeffler serum positive results were obtained only in 16·76 per cent. of the same cases. Of these, 29·04 per cent. were positive only by the use of the author's methods, without which they would not have been recognized as cases of diphtheria. Another important result obtained by the new methods was the identification of *B. diphtheriae* in a number of cases which had recovered from the malady for a considerable period of time. The methods are, therefore, particularly recommended for the identification of carriers. C. D. F.

Gaviati, A. Nuovo contributo sull' infezione erpetica sperimentale. [**Fresh investigations on experimental herpetic infection.**] *Riforma med.*, 1922, **38**, 713.

By inoculating either the contents of herpetic vesicles or the fluid from the experimental herpetic kerato-conjunctivitis on to the nasal mucous membrane of rabbits the picture of the herpetic general infection was consistently obtained. C. D. F.

Spiller, W. G. Epidemic encephalitis with myelitis. *Arch. Neurol. & Psych.*, 1922, **7**, 739.

von Weizsäcker, V. Ein ungewöhnlicher, perakut verlaufender Fall von multipler Sklerose mit anatomischem Befund. [**Unusually acute case of multiple sclerosis with post-mortem findings.**] *Monatschr. f. Psych. u. Neurol.*, 1921, **49**, 221.

Spiller's case is interesting because the symptoms suggested at first a brain tumour, and because the histo-pathological examination of the spinal cord showed the existence of lesions similar to those of multiple sclerosis. By means of Weigert's method many sclerotic patches were found, not only in the spinal cord but also in the medulla oblongata, pons, and mid-brain. The author, however, came to the conclusion that it was a case of 'epidemic encephalo-myelitis' because of the presence of intense perivascular infiltration by lymphocytes, plasma cells, neuroglia cells, and fatty granular cells.

The case previously published by v. Weizsäcker was characterized by similar histological alterations, but the conclusions reached were different. The patient, aged 57, had had syphilis at the age of 17, and received six courses of treatment. Eight years previously he had had transient diplopia. Eight days before admission into hospital he complained of headache, weakness, instability of gait, weakness of the hands, and a dead feeling in the little finger. Then diplopia reappeared and hiccough began. On admission fever, cyanosis, and stupor were noticed. The examination of the cerebrospinal fluid gave the following results: globulin increased, cell count, 20 (lymphocytes). Wassermann test, negative. The Wassermann test of the blood was also negative. The temperature rose to 39° C. and the stupor gradually deepened. There was muscular rigidity and the face was somewhat mask-like, but the reflexes remained normal. Death ten days after the onset of symptoms. At the post-mortem examination no evidence of syphilis was found. In the white matter of the cerebrum, pons, cerebellum and medulla oblongata, a small number of sclerotic patches were noticed which did not differ from the plaques of long-standing multiple sclerosis. In addition there was an acute process most marked in the pons and medulla, but extending to the cervical and dorsal portions of the spinal cord. This was characterized by a great number of foci of ganglion cell degeneration, intense neuroglia proliferation, and so-called neuronophagia. Round the blood-vessels of the affected areas there was an intense small-celled infiltration consisting chiefly of lymphocytes, which in places were spreading into the tissue. A new formation of capillaries was likewise noticed. These acute changes superimposed upon chronic ones were difficult to interpret, since they did not essentially differ from those described in cases of acute multiple sclerosis, acute encephalitis, and especially of lethargic encephalitis. However, the author felt justified in considering the case as one of multiple sclerosis because of the typical plaques in the white substance with scanty involvement of the cerebral cortex and definite proliferation of the neuroglia. C. D. F.

Schaller, W. F., and **Oliver, J. Chronic epidemic encephalitis.** *Arch. Neurol. & Psych.*, 1922, **8**, 1.

Report on clinical and anatomical findings in a case extending over a period of fourteen months. From both standpoints no evidence was found of a healed process with disturbance of function from destroyed structures, but of a continuously progressive process. This was particularly shown by the histological investigation. In the same regions, areas of gliosis were found with amylaceous bodies where the process was quiescent, and other areas in which most acute inflammatory changes were present. The cerebral cortex (gyrus centralis anterior and posterior), the cerebellum, and caudate nucleus showed no lesions, while the optic thalamus and substantia nigra were most affected. In these regions, besides intense perivascular infiltrations and perivascular haemorrhages, areas of neuroglia proliferations were noticed. In the optic thalamus the nerve-cells were mostly affected, the lesions consisting of chromatolysis, shrinkage and vacuolization, as well as of fragmentation of the intracellular neurofibrils. According to the authors their case is similar to that described by v. Economo (*Vien. Arch. inn. Med.* 1920, **1**, 371), in which the disease extended over a period of two years. The type of lesions was the same even as regards the peculiar areas of sponge-like gliosis. In Economo's case, however, these were in the cerebral cortex with a resulting secondary degeneration of the pyramidal tract. C. D. F.

FRANCO, E. E. Contribuzione alla conoscenza dell' anatomia patologica della Leishmaniosi cutaneo-mucosa od americana. [**On the morbid anatomy of dermal Leishmaniosis.**] *Arch. per le sc. med.*, 1922, **44**, 246.

The case investigated by the author appears to be the only one of dermal Leishmaniosis so far observed in Portugal. The patient had contracted the disease in Brazil five years before his death, which was apparently caused by a severe form of phthisis. The lesions due to the Leishmaniosis were spread over the skin of almost the whole body, but particularly that of the face and the mucous membranes of the first tract of the alimentary canal and respiratory passages. No Leishmaniotic lesions of the internal organ were observed. The alterations of the affected areas of the skin and mucous membranes were characterized by a new production of connective tissue with perivascular infiltrations consisting chiefly of small cells of the lymphocytic type and a few plasma cells. No giant cells were seen, but a considerable number of macrophages. These were in part irregularly distributed in the inflammatory tissue, in part situated next to or within the infiltrated blood-vessels. Many Leishman-Donovan bodies were found in the affected areas, particularly within the macrophages, sometimes together with ingested red blood corpuscles. C. D. F.

DE BUEN, F., e **DE BUEN, S.** Nota sull' acclimatazione della *Gambusia affinis*. [**Note on the acclimatization of *Gambusia affinis*.**] *Ann. d'ig.*, 1922, **32**, 281.

Gambusia affinis (top-feeding minnow) has been successfully used in the United States of America to destroy mosquito larvae in stock ponds and similar breeding-places. The authors describe an attempt at acclimatizing this small fish in an aquarium, some ponds, and small rivers of Talayuela (Spain), where other antimalarial measures were tried at the same time. The *Gambusia* multiplied only in the rivers and ponds communicating with them during the rainy season. C. D. F.

Carpano, M. La trasmissione placentare della piroplasmosi. **[Placental transmission of piroplasmosis.]** *Ann. d'ig.*, 1922, **32**, 286.

Infections due to haemosporidia, but particularly that due to *Nuttalia equi* may be transmitted through the placenta from the mother to the foetus even if the former has been infected some years before pregnancy took place and no apparent trace of the infection is left. Such cases prove the existence of a congenital piroplasmosis, which may be the cause of death of the foetus and of abortion. C. D. F.

Castelli, A. Sulla divisione delle forme anulari dei parassiti malarici. **[On the division of annular forms of the malaria parasites.]** *Ann. d'ig.*, 1922, **32**, 259.

In some cases the annular forms of the malaria parasite may multiply within the red blood corpuscles, within which as many as ten young parasites are seen. In the case described by the author, a two-year-old baby affected by tertian fever, the fact was particularly plain and was observed for 12 hours. C. D. F.

Grassi, B. Animali domestici e malaria. Nuovo orizzonte nella lotta antimalarica. **[Domestic animals and malaria. New horizon in the antimalarial struggle.]** *Ann. d'ig.*, 1922, **32**, 421.

In this large memoir Grassi summarizes the results of investigations carried out since 1918. It is subdivided into four chapters with an appendix and a summary from which the following conclusions are taken: in places inhabited by men and domestic animals, mosquitoes (*Anopheles claviger*) bite the latter more frequently than the former. Stalls and pigsties, particularly if without windows and unventilated, are the favourite shelter for mosquitoes, which find there the warmth necessary for the development of malarial parasites. The number of mosquitoes existing in a determined place is, in the main, dependent on the number of 'anopheligenous foci' and appears to increase in proportion to the number of inhabitants of that place. Mosquitoes may migrate for miles in search of food, and seem to be attracted to certain places by the presence of domestic animals. Also in regions most affected by malaria the zoophilia of mosquitoes is quite remarkable. The phenomenon of anophelism without malaria can be explained only by assuming a 'misanthropy' of mosquitoes in certain places and conditions. It is not excluded, however, that other factors may play a rôle in the production of the phenomenon. For instance, a low night temperature may be particularly favourable to the accumulation of the mosquitoes in stalls and pigsties. Whether there are mosquitoes which bite man in preference to animals, or only certain kinds of animals, is a question which cannot at present be answered definitely. The same uncertainty exists as to the question whether mosquitoes which have bitten man afterwards bite man only. C. D. F.

Ravenna, E. Endocardite da carbonchio sintomatico e endocardite tossica sperimentale. **[Endocarditis from *B. anthracis symptomatici* and experimental toxic endocarditis.]** *Arch. per le sc. med.*, 1922, **44**, 268.

In the spontaneous infection from *B. anthracis symptomatici* occurring in cattle (oxen), acute endocarditis is almost constant. The principal localization is, as a rule, in the right auricle, but may extend to the aortic and mitral valves. A similar affection is experimentally obtainable in guinea-pigs by intravenous inoculations of either living or filtered liver-bouillon cultures of *B. anthracis symptomatici.* C. D. F.

Tunnicliff, Ruth, and **Moody, W. B. Experimental measles by inoculation of monkeys, guinea-pigs, and rabbits with a green-producing diplococcus.** *J. Infect. Dis.*, 1922, **31**, 382.

One of the authors (Tunnicliff) described in 1917 the existence of a small Gram-positive diplococcus yielding green colonies on aerobic blood agar plates. This microbe was grown from the blood, eye, nose, throat, and sputum of patients with measles during the pre-eruptive and early eruptive stage of the disease. The diplococcus was pathogenic for the rabbit, dog, mouse, and rat, but not for the guinea-pig, when injected intravenously or intraperitoneally, but no rashes or symptoms of measles were observed. The authors, in the present paper, describe the effects of intratracheal injections, and find that monkeys, guinea-pigs, and rabbits are susceptible to measles when inoculated with the washings of the nose and throat of patients with measles. The same symptoms and lesions may also be produced in these animals by the green-producing diplococci above described. Rabbits successfully inoculated with washings or the diplococcus showed no symptoms when re-inoculated. Green-producing diplococci from the lungs and blood of rabbits successfully inoculated with diplococci from measles produce Koplik spots and exanthems when injected into other rabbits. While the experiments indicated that the reaction was due to the diplococcus itself and not to a separate virus carried with it, on account of the same symptoms being produced by cultures as late as the seventh generation and the absence of reaction in rabbits injected with other bacteria isolated from the same plate as the green-producing diplococci, the authors considered it possible that the diplococcus possessed the selective power of carrying the specific virus of measles. W. B.

Flexner, S. Experimental epidemiology. Introductory. *J. Exper. M.*, 1922, **36**, 9.

Lynch, Clara J. An outbreak of mouse typhoid and its attempted control by vaccination. *J. Exper. M.*, 1922, **36**, 15.

Amoss, H. L. (1). **An artificially introduced epidemic of mouse typhoid.** *J. Exper. M.*, 1922, **36**, 25.

Amoss, H. L. (2). **Effect of the addition of healthy mice to a population suffering from mouse typhoid.** *J. Exper. M.*, 1922, **36**, 45.

Webster, L. T. (1). **Experiments on normal and immune mice with a bacillus of mouse typhoid.** *J. Exper. M.*, 1922, **36**, 71.

Webster, L. T. (2). **Identification of a paratyphoid-enteritidis strain associated with epizootics of mouse typhoid.** *J. Exper. M.*, 1922, **36**, 97.

Amoss, H. L., and **Haselbauer, P. P. Immunological distinctions of two strains of the mouse typhoid group isolated during two spontaneous outbreaks among the same stock.** *J. Exper. M.*, 1922, **36**, 107.

In this series of papers, Flexner and his co-workers at the Rockefeller Institute record the results obtained in the initial stages of an attempt to apply the experimental method to the study of the epidemic spread of infection.

In his introductory paper, Flexner briefly reviews the present position of epidemiology. He notes the tendency, evidenced in some quarters, to return to the older explanations, vaguer and more mystical though they be, and emphasizes the need for the bacteriologist to justify his belief in specific aetiology, by widening and deepening his search for the factors which determine the phenomena of epidemics. Flexner then considers the various factors which appear to play a part in the experimental epidemics observed by his co-workers, and refers especially to the lability of the bacterial parasites, the variations in the resistance of the animal hosts, and the effects produced by variations in 'dosage'.

Lynch describes the large epidemic, arising spontaneously among a stock of about 3,000 mice, which formed the starting-point of these investigations. The epidemic lasted over about 2½ years, with two major and one or more minor waves of mortality. The records suggest that each of the larger waves is, in reality, composed of several smaller fluctuations, running into and partially superimposed upon one another. During the entire period of the epidemic the population was being augmented by fresh births, so that the rapid fall in total numbers during a large wave of mortality was followed by a slow rise, caused by the excess of the births over the deaths in the inter-epidemic period. Serological examination of strains isolated during the first large outbreak, and their comparison with other strains isolated during the second outbreak, showed that the two sets of strains were serologically distinct. Vaccination of a portion of the mice exposed to risk had been carried out during the inter-epidemic period; but it is not possible to estimate how far this may have been responsible for the change in type of the bacterial parasite concerned.

Amoss, in the first of his communications, describes his general method of procedure, which consisted in keeping the mice in small cages, each containing five animals, and allowing infection to be spread by the attendant during the routine of feeding and cleaning. The mice in certain cages were fed upon cultures of *B. typhi murium.* Other cages of normal mice were brought into the animal-house from time to time and arranged in various ways. Sometimes there was rapid and extensive spread from the infected to the healthy cages; at other times such spread was delayed or failed to occur to any wide extent.

Experiments are recorded, designed to determine the virulence of strains isolated from single bacterial cells, when injected intraperitoneally and when administered by the mouth. Such single-cell strains were also employed for a few experiments in which mice were exposed to the risk of infection in the manner described above. The facts are recorded without any attempt to draw conclusions from them, since the evidence is considered to be insufficient.

In his second paper, Amoss describes a larger series of experiments in which normal mice were introduced at intervals into an animal-house in which cage-to-cage infection was occurring. In most cases the addition of new mice was so arranged as to replace, by normal individuals, the mice which had succumbed to infection since the last addition of normals. By proceeding in this way, Amoss found that the exposure of normal mice to others infected by feeding usually led to the occurrence of sporadic deaths, whereas the addition of further normals was followed, not by more sporadic deaths, but by an epidemic outbreak, during which many of the older mice succumbed.

Each such outbreak came to an end after a certain time, leaving a varying proportion of survivors. Further additions of normal mice were followed by fresh outbreaks. In the course of these there was a definite tendency for the newcomers to die before the older inhabitants, but the latter only outlived the former by relatively short periods. Amoss concludes that an essential factor in the epidemic spread of infection is the accumulation of sufficient susceptibles.

Webster has studied the resistance to infection with mouse-typhoid bacilli, exhibited by normal and by immunized mice. The results recorded indicate that immunization by intraperitoneal inoculation gives rise to an increased resistance, evidenced by a lengthening of the period elapsing between infection and death, when such vaccinated mice are inoculated, along with normal controls, with living cultures of the same organism. Subcutaneous inoculation of killed cultures results in a similar partial immunization against the effects of subsequent administration of living bacilli either *per os* or by intraperitoneal inoculation. Feeding mice with living or with killed cultures affords a definite degree of protection against intrastomachal or intraperitoneal inoculation of living bacteria. In all these cases the evidence points to the immunity being general rather than local. Agglutinins were demonstrated in the blood-stream in many cases. In no case was there any evidence of a local immunity. Thus, after injections of killed cultures into one pleural cavity, inoculation with living cultures produced identical results whether made into the previously treated pleural cavity or into the peritoneum.

In a second paper, Webster reports a serological study of the strain which was utilized in these experiments and in those of Amoss. The results of direct agglutination tests with 13 paratyphoid strains and the corresponding antisera, followed by absorption experiments, served to identify the organism in question with *B. pestis caviae* (Smith), and to show its very close relationship to *B. aertrycke* (Mutton).

Amoss and Haselbauer record the results obtained in a serological examination of the strains isolated during the earlier and later stages of the epidemics described by Lynch. The former strains were found to be closely related to *B. enteritidis* (Gärtner), the latter to *B. paratyphosus* B. The strains studied by Webster came from this latter series.

With the exception of Flexner's introductory paper, this series of reports consists mainly of a record of observations. These observations form a valuable addition to the data which, in this unexplored field of experimental medicine, must form the basis for future generalizations. It is satisfactory to record that Flexner's contribution contains a statement that these experiments are being continued and extended in their scope.

W. W. C. T.

BIOCHEMISTRY

McCollum, E. V., Simmonds, N., Becker, J. E., and **Shipley, P. G. Studies on experimental rickets. XXI. An experimental demonstration of the existence of a vitamin which promotes calcium deposition.**

McCollum, E. V., Simmonds, N., and **Becker, J. E. On a type of ophthalmia caused by unsatisfactory relations in the inorganic portion of the diet. An ophthalmia not due to starvation for fat-soluble A, and not curable by its administration.** *J. Biol. Chem.*, 1922, **53**, 313.

The fat-soluble vitamin which cures xerophthalmia is not the same as that which promotes the growth of bones. The evidence for this view is as follows: Cod-liver oil after several hours' oxidation will not cure xerophthalmia in rats; it will, however, still promote the deposition of calcium in the bones of young rats suffering from rickets. Coconut oil will not cure xerophthalmia, but again will promote the deposition of calcium salts in rickets. Olive oil will do neither. Butter fat contains the calcium depositing factor in less quantity than cod-liver oil. It is therefore necessary to postulate another fat-soluble vitamin.

In the second paper the importance of a proper balance of salts in the diet becomes emphasized by the discovery that diets containing very high contents of chlorine may induce an eye condition closely simulating the xerophthalmia due to lack of fat-soluble A. R. A. P.

Telfer, S. V. Studies in calcium and phosphorus metabolism. i. The excretion of calcium and phosphorus. *Quart. J. Med.*, 1922, **61**, 45.

The excretions of calcium, phosphorus, and fatty derivatives are interdependent: 20 to 30 per cent. of the total CaO excreted is present in the form of calcium soaps. The total calcium and phosphorus eliminated is nearly proportional to the intake, no evidence being obtained that mineral matter from endogenous sources is excreted in the faeces to an appreciable extent. An excess of calcium in the ingesta restricts an increased amount of phosphorus to the intestine: with low intakes of fat and phosphorus, an excess of calcium in the diet may render the urine phosphorus free. With a persistent excess of fatty acids in the intestine, a much greater proportion of calcium is excreted as soaps. The faecal solids of infants are derived in large part from the diet. The average faecal weight depends chiefly on the degree to which calcium soap formation occurs, these soaps acting mechanically by incorporating in their mass fatty derivatives, &c. All observations seem to indicate that the greater part of the calcium intake is restricted to the gut: and except the small amount excreted in the urine the amount absorbed is nearly equivalent to the amount retained. In normal infants 40 per cent. of the total phosphorus is excreted in the urine, 60 per cent. in the faeces: with excess of fatty acids in the faeces more phosphoric acid is deviated to the urine. O. L. V. de W.

Telfer, S. V. Studies in calcium and phosphorus metabolism. II. The metabolism of calcium and phosphorus in rickets. *Quart. J. Med.*, 1922, **61**, 63.

In normal infants an excess of P_2O_5 is retained over the equivalent amount of CaO required for bone formation. In cases of rickets there were diminished retentions of both bodies, but the defect in P_2O_5 retention was the more pronounced. The author suggests that the diminished retention of P_2O_5 was not due to a lessened absorption of phosphorus, but to a diminished fixation by calcium, the absorption of the latter being defective. He believes that this impaired absorption of calcium, due possibly to some alteration in the gastro-intestinal functions, cannot be excluded as a factor in the causation of bone softening in rickets. No negative balances of CaO or P_2O_5 were noted, and no evidence was therefore obtained for excessive decalcification as the cause of the bony lesions of rickets. O. L. V. de W.

Sherman, H. C., and **Hawley, E.** **Calcium and phosphorus metabolism in childhood.** *J. Biol. Chem.*, 1922, **53**, 375.

This laborious series of experiments upon children emphasizes the importance of a large supply of milk in the diet. Children aged 3–13 years, who were taking daily 750 gm. of milk, stored approximately 0·01 gm. of Ca per kilo per day. The storage of Ca could be increased by increasing the daily supply of milk to 1,000 gm., optimum storage taking place when about 1 gm. per day of Ca was being given. This means that the child requires more calcium than the adult. The calcium in vegetables is not so readily available. R. A. P.

Schiff, E., u. **Kochmann, R.** Zur Pathogenese der Ernährungsstörungen beim Säugling. [**Pathogenesis of nutritional disturbances in infancy.**] *Jahrb. f. Kinderh.*, 1922, **99**, 181.

Bacillus coli, besides its fermentative activities, is able to split proteins with amine formation. The predominance of either process is determined by the reaction of the medium. The processes are not mutually exclusive, and the classical contradistinction between fermentation and putrefaction does not exist in fact. It is suggested that the intoxications accompanying severe digestive disturbances in young children are due to absorption of these amines. The fat intolerance noted in digestive disturbances is due to the fact that fats and the salts of the higher fatty acids give a marked impetus to bacterial growth. Histamine and choline are not destroyed in blood. O. L. V. de W.

Findlay, G. M., and **Mackenzie, R.** **Opsonins and diets deficient in vitamins.** *Biochem. J.*, 1922, **16**, 574.

In an attempt to ascertain whether the death from intercurrent bacterial infections in animals fed on a diet lacking in vitamins is due to a lowering of the opsonic activities of the serum, the authors have examined this point and come to the conclusion that no deficiency in opsonic activity is to be found in avitaminosis. C. G. L. W.

Drummond, J. C., **Crowden, G. P.**, and **Hill, E. L. G.** **Nutrition on high protein dietaries.** *J. Physiol.*, 1922, **56**, 413.

Experiments on rats and kittens. For the rats, the diet consisted of 83 per cent. caseinogen with the addition of vitamins A, B, and C, and salt mixture. Growth was almost normal until the end of the first month, after which definite retardations occurred. On changing to a normal diet the animals reached a normal weight. The rats remained in good health, but did not reproduce. No damage to the kidneys results from the excessive demand for excretion of nitrogenous waste products. The organs and tissues were normal in appearance at the end of the experiment.

O. L. V. de W.

Tisdall, F. F. The influence of the sodium ion in the production of tetany. *J. Biol. Chem.*, 1922, **54**, 35.

Gross, E. G., and **Underhill, F. P. The metabolism of inorganic salts. I. The organic ion balance of the blood in parathyroid tetany.** *J. Biol. Chem.*, 1922, **54**, 105.

The injection of dibasic sodium phosphate into dogs gave the following changes in the serum, namely, a reduction of the calcium, an increase of the inorganic phosphorus, and in one case a slight alkaline change of the reaction. The injection of phosphoric acid was followed by the same changes in the calcium and phosphorus, but there was a decided reduction in the sodium and the CO_2 combining power of the serum, as well as a definite increase in its acidity. These facts are against the view that the calcium-phosphorus ratio has any influence upon the production of tetany, and, leaving out of consideration the gastric type, support the view that the important factor is the sodium calcium ratio. (Tetany was not produced when the Na bicarbonate was lowered.)

The paper by Gross and Underhill naturally lends itself for discussion with the above. An investigation of the tetany following removal of the parathyroids in dogs has led them to the opinion that there is a marked change in the K/Ca ratio; convulsions are produced when this ratio exceeds 10. This makes it appear that there is something in the old view of the connexion of parathyroid tetany with calcium. It will be remembered that Paton and Findlay have brought forward evidence in support of the view that in parathyroid tetany the toxic substance guanidine accumulates in the blood. The relation between these two abnormalities, which occur in animals with parathyroid tetany, does not yet seem to be clear. R. A. P.

Fleming, G. B. The respiratory exchange in cretinism and Mongolian idiocy. *Quart. J. M.*, 1922, **61**, 11.

In the untreated cretin the basal metabolism is unduly low, but is raised to a normal level by thyroid treatment. In six Mongolian idiots the basal metabolism was found to be normal, and thyroid treatment had no effect.

O. L. V. de W.

Rypins, H. The distribution of metabolites in blood and tissues. *Arch. Int. Med.*, 1922, **30**, 578.

Estimations of sugar, urea, and creatinine in blood, and pleural and ascitic transudates and exudates, and in cerebrospinal fluids. In cases with a normal blood metabolite level, serous effusions showed a sugar content amounting to 83 per cent. of the content of the blood, urea 80 per cent., and creatinine 67 per cent. The corresponding concentrations in cerebrospinal fluid were sugar 44 per cent., urea 58 per cent., and creatinine 68 per cent. of the blood content. With increasing blood metabolite levels the concentration in the fluids varied *pari passu*. No characteristic difference in the metabolite concentration of transudates and exudates was observed.

O. L. V. de W.

Bohne, C. Beiträge zur chemischen Kinetik der Kohlenhydratverdauung im Duodenum der Säugetiere. [**The kinetics of carbohydrate digestion in the mammalian duodenum.**] *Fermentforschung*, 1922, **6**, 200.

It has been shown that the pancreatic diastase differs from other ferments of the same type in being more sensitive to other ions than hydrogen or hydroxyl, and the author has investigated the effects of phosphates, sodium chloride and carbonates, on the activity of the ferment. While both carbonates and phosphates can activate a ferment which is further influenced by the addition of sodium ions and chlorine ions in sodium chloride, the chlorine promotes digestion and can depress the inhibiting action of the hydrogen and especially the hydroxyl ions.

C. G. L. W.

Hill, E., and **Bloor, W. R.** **Fat excretion.** *J. Biol. Chem.*, 1922, **53**, 171.

Previous workers have shown that there is much fat in the faeces which does not come from the food. It arises either from breakdown of cellular material, or of bacteria, or by simple excretion from the intestine. The question has been tested by the authors upon cats, using fats of widely different composition such as olive oil and coconut oil. While the iodine value of the faecal fat on the olive oil diet was higher than that upon the coconut oil, it did not approach that of the oils themselves, but rather that of the fat free diet. This indicates that the greater part of the faecal fat is not derived from the food, and invalidates experiments in which the degree of utilization of food fat is judged from the fat contents of the faeces, independently of estimations of the fat upon fat free diets. R. A. P.

Atkinson, H. V., Rapport, D., and **Lusk, G.** **Animal calorimetry. The production of fat from protein.** *J. Biol. Chem.*, 1922, **53**, 155.

Using his well-known methods, Lusk and his co-workers conclude that, in the dog, when the glycogen reserves are low, excess of meat is converted into glycogen. If the ingestion of meat is excessive there is in addition a deposition of fat. Fat alone is retained when the ingestion of meat is in very large excess, that is under abnormal conditions. The production of fat from protein may be inferred from the respiratory quotient. Attention is given in this paper to the problem of 'deposit' protein, the protein which is retained upon excessive meat diets, and which leads to an increase in the basal metabolism. The basal metabolism after cessation of the meat feeding gradually falls with elimination of this 'deposit'. R. A. P.

Gottschalk, A., u. **Pohle, E.** Untersuchungen über den Mechanismus der Adrenalinhyperglykämie. I. u. II. Mitteilung. [**Investigations into the mechanism of adrenalin hyperglycaemia; I and II.** *Arch. f. exper. Path. u. Pharmakol.*, 1922, **95**, 65, 75.

In these two papers a demonstration is given of the following series of points: (1) If the abdomen of a rabbit be opened under local anaesthesia with novocaine, so that access to the portal vessels is obtained, then coincidently with the rise of blood-sugar produced by intravenous injection of adrenalin, a rise in the hydrogen-ion concentration of the blood may be demonstrated, using for the latter measurement the method of the gas chain. (2) Temporary occlusion of the portal vein by a ligature causes, after the release of the vein, a rise in the C_H and a rise in the blood-sugar. (3) Temporary occlusion of the portal system from the general circulation delays, so long as the occlusion lasts, the effect of adrenalin in causing a rise of blood-sugar. (4) Oral administration of sodium bicarbonate (180 c.cm. of 6 p.c.) prevents the rise of C_H seen after an injection of adrenalin intravenously, and greatly depresses the rise in the blood-sugar. It is concluded that the rise of blood-sugar caused by adrenalin is due to a rise in the C_H of the blood in the portal area. J. H. B.

de Huan, J. The renal function as judged by the excretion of vital dyestuffs. *J. Physiol.*, 1922, **66**, 444.

Ultrafiltration shows that the greater part by far of the acid vital dyestuffs is adsorbed by the colloids of the plasma. From a comparison of concentrations of urea and dyes in plasma with the corresponding concentrations in the urine, the author concludes that the primary glomerular filtrate cannot be free from protein. O. L. V. de W.

Verney, E. B., and **Starling, E. H. On secretion by the isolated kidney.** *J. Physiol.*, 1922, **56**, 353.

A method is described of supplying arterial blood to the isolated kidney by means of a heart-lung preparation. A good flow of urine may be obtained under these conditions, and this is not a mere transudate since its urea or glucose content may be many times that of the circulated blood. The limiting blood-pressure for secretion was found to be 40 mm. Hg; this was lowered by dilution of the blood, and the limit is regarded as due to the osmotic pressure of the blood colloids. Normal saline, urea and sodium sulphate exert a diuretic effect on the kidney under these conditions, without any corresponding increase in the blood flow. In all the experiments the urine secreted was hypotonic, owing apparently to retention of chlorides, and alkaline in reaction. This may be due to over-ventilation.

O. L. V. de W.

Davies, W. H., **Haldane, J. B. S.**, and **Peskett, G. L. The excretion of chlorides and bicarbonates by the human kidney.** *J. Physiol.*, 1922, **56**, 269.

The maximum possible molecular concentration of chlorides in the urine (for J. B. S. H.) is about 0·33 N.: the bicarbonate maximum has the same value. If both ions are being excreted together the sum of their molecular concentrations has this same value. The maximum is independent, within wide limits, of the total molecular concentration of the urine, or those of the urea and phosphates. O. L. V. de W.

Blatherwick, N. R., and **Long, M. L. Studies of urinary acidity. i. Some effects of drinking large amounts of orange juice and sour milk.** *J. Biol. Chem.*, 1922, **53**, 103.

The taking of large amounts of most fruits leads to the formation of less acid urine, owing to the oxidation of the organic acids and the excretion of the basic substances in the urine. The authors have tried to see whether it is possible to overstep the powers of the organism in this particular. Using as their subjects two young healthy women, it was found that the drinking of large amounts of orange juice (even up to a citric acid equivalent of 48 gm. in the day), led to alkaline urines, together with an increased organic acid excretion and a decreased ammonia content in the urine, so that it is not easily possible to overreach the capacity of the body to deal with fruit juices. The taking of large quantities of milk containing lactic acid led on the contrary to acid urine. R. A. P.

Nassau, E. Über die Bedeutung der Reaktion des Harnes für das Auftreten der statischen Albuminurien im Kindesalter. [**Significance of reaction of the urine in the production of orthostatic albuminuria in childhood.**] *Ztschr. f. Kinderh.*, 1921, **33**, 158.

Functional static albuminuria in children is abolished by administration of alkalis. This phenomenon is explained on the lines of Fischer's work, as being due to the neutralization of acids which are produced in the congested kidney. Evidence is produced that the acidity of the urine rises in these children, after the lordotic position has been maintained for 10–15 minutes.
O. L. V. de W.

Lüscher, E. The nitrogen distribution in Bence-Jones protein, with a note upon a new colorimetric method for tryptophan estimation in protein. *Biochem. J.*, 1922, **20**, 556.

The nitrogen distribution of Bence-Jones protein was determined by van Slyke's method. The Bence-Jones protein is a substance which differs from all other proteins which have hitherto been analysed, not only in its physical behaviour, but in the distribution of its nitrogen, and it would appear that the substance is the same in all cases of Bence-Jones proteinuria.
C. G. L. W.

Addis, T., and **Foster, M. G.** **The specific gravity of the urine.** *Arch. Int. Med.*, 1922, **30**, 555.

The specific gravity of the urine is the resultant of the various effects of different urinary constituents. Since each of these has its own specific effect, no precise significance attaches to any method of estimating the total solids of the urine by specific gravity measurements. This point is illustrated by experiments on restriction of fluids, and on administration of various salts and urea. Not even an approximate idea of the work done by the kidney could be formed from the specific gravity results.
O. L. V. de W.

Addis, T., and **Shevky, M. C.** **A test of the capacity of the kidney to produce a urine of a high specific gravity.** *Arch. Int. Med.*, 1922, **30**, 559.

In normal individuals under the conditions described the specific gravity on the average reaches 1032. The importance of the principle of strain in testing renal function is emphasized. O. L. V. de W.

Means, J. H., and **Burgess, H. W.** **The basal metabolism in non-toxic goitre, and in borderland goitre cases.** *Arch. Int. Med.*, 1922, **30**, 507.

A study of 1,000 cases. A group of 102 clinically non-toxic goitre cases showed, from the point of view of basal metabolism, a high grade of normality. In 16 only of these cases was the deviation from normal greater than ± 10 per cent. Provided that fever, acromegaly, leukaemia and severe anaemia can be excluded an increased basal metabolism is strong presumptive evidence of hyperthyroidism. Similarly if starvation, hypopituitarism and hypo-suprarenalism are excluded a low rate of basal metabolism is evidence of hypothyroidism. Errors in the determination are in the direction of giving too high values. If necessary, the test should be repeated until constant readings on different days are obtained.

O. L. V. de W.

Bayliss, W. M. Haemorrhage and blood volume. *J. Physiol.*, 1922, **56**, xlvi.

If not more than 70 per cent. of the calculated blood-volume is removed it can be effectively replaced by gum saline, so far as any signs of respiratory or other failure is observed. A loss of 30 per cent. is fatal in 2 to 3 hours, if not replaced.

O. L. V. de W.

Van Slyke, D. D., Austin, J. H., and **Cullen, G. E. The effect of ether anaesthesia on the acid base balance of the blood.** *J. Biol. Chem.*, 1922, **53**, 277.

These experiments were done to clear up a discrepancy in the literature. Menten and Crile, and others had shown that rabbits reacted to ether anaesthesia with a fall in P_H of the blood. Caldwell and Cleveland found a fall in plasma bicarbonate in patients as a result of ether anaesthesia. On the other hand, Yandel Henderson and Haggard considered that there first occurred an alkalosis due to the blowing off of CO_2 from the blood, with subsequent compensation by the shift of base from the blood to the tissues.

In these experiments the P_H, and the alkaline reserve were measured together. The results showed that ether anaesthesia leads to a more acid reaction of the blood as well as a concurrent fall in the alkaline reserve. This means that there occurs either the addition of acid to the blood or the withdrawal of base from the blood under ether anaesthesia, an acidosis rather than an alkalosis.

R. A. P.

Randles, F. S., and **Knudson, A. The estimation of lipoid phosphoric acid in blood by application of the Bell and Doisy method for phosphorus.** *J. Biol. Chem.*, 1922, **53**, 53.

Certain advantages are claimed over the Bloor method for the determination of the lecithin substances in the blood. In the method as used, blood is shaken with an alcohol ether mixture, a convenient portion of the filtrate is evaporated to dryness and digested for 10 minutes with a nitric-sulphuric acid mixture. Molybdic acid solution and hydroquinone are added, and after mixing and allowing to stand, alkaline sulphite solution. A colour comparison is then made against a standard. The method is claimed to be rapid and to give as good results as the other methods.

R. A. P.

Henning, B. H. The lipoids of the blood in tuberculosis. *J. Biol. Chem.*, 1922, **53**, 167.

A consideration of the lipoid nature of the tubercle bacillus makes a study of the lipoid content of the blood in tuberculous patients of some interest. The total fatty acid and the lecithin were found to be within the normal range. The residual fatty acid was high. Some change had occurred in the cholesterol, which was found to be low when estimated by the saponification method, but normal when estimated without saponification. This seems to indicate the presence of some new substance in tuberculous blood closely related to cholesterol. R. A. P.

Terrill, E. On the colorimetric determination of haemoglobin, with especial reference to the production of stable standards. *J. Biol. Chem.*, 1922, **53**, 179.

Attention is given to several points in connexion with the Sahli method of estimation, in especial the preparation of the stock solutions of acid haematin. R. A. P.

Kramer, B., and **Tisdall, F. E. The distribution of sodium, potassium, calcium, and magnesium between the corpuscles and serum of human blood.** *J. Biol. Chem.*, 1922, **53**, 241.

There is no sodium in the blood corpuscles. The concentration of potassium is 428 mgm. per 100 c.cm. of corpuscles. Only about 2–4 mgm. of magnesium are present in 100 c.cm. of corpuscles, and practically no calcium. From this it can be concluded that sodium represents about 92 per cent. of the fixed base of the serum, and potassium practically all of the fixed base of the corpuscles. It would be interesting to know the reason for the presence of so special a base in the corpuscles. R. A. P.

Fleisch, A. Blutgasanalysen bei geschädigter Gewebeatmung; ein Beitrag zum Wesen der Vogelberiberi. [**Blood gas analyses in pathological tissue respiration; a contribution to the nature of avian beri-beri.**] *Arch. f. exper. Path. u. Pharmakol.*, 1922, **95**, 17.

The author has investigated the amounts of oxygen and carbon dioxide in the arterial and venous blood of pigeons suffering from polyneuritis, and compared these amounts with those of normal pigeons. In normal birds there was a difference of 8 volumes per cent. between the oxygen in the arterial and venous blood; in birds with beri-beri, this difference was only 4·6; the CO_2 difference in normal birds of 4·5 became, in the beri-beri cases, 3·3. The normal body temperature of 41·6° C. became 35° C., and the haemoglobin value of 75 (normal) became 62. These figures represent average results; 3 birds were used to obtain the normal values, and 5 to obtain the beri-beri values. J. H. B.

Müller, C. Die Messung des Blutdrucks am Schlafenden als klinische Methode. [**Measurement of the blood-pressure during sleep.**] [**B.**] *Acta Med. Scand.*, 1921, **55**, 381–485.

Blume, P. Om Blodtrykket hos sovende. [**The blood-pressure during sleep.**] *Ugesk. f. Læger.*, 1922, **84**, 1126–32.

At the Communal Hospital in Christiania, Müller has carried out extensive blood-pressure measurements on adults and children while asleep. The b.p. of the normal person while he is awake varies greatly from time to time, and it is, therefore, difficult to fix the limits beyond which the b.p. must be regarded as abnormally high. Even at rest, the b.p. shows considerable oscillations, which are largely determined by psychic factors.

These and other disturbing factors are almost wholly eliminated during sleep, and Müller found that among 34 healthy men the systolic b.p. was about 94 mm., and among 30 healthy women it was about 88 mm. It seldom varied by more than 5 mm. from this average, and never by more than 9 mm. The b.p. among 33 children between the ages 3 and 14 years varied with age, being 64 mm. up to the age of 5, 75 mm. up to the age of 10, and 80 mm. between the ages 11 and 14. The constancy of the level of the b.p. among sleeping adults was unaffected by the height of their b.p. when they were awake. It would, therefore, seem that the stability of the b.p. is very much greater during sleep than at other times.

Blume has checked these investigations, measuring the b.p. during sleep of 50 patients at the Communal Hospital in Copenhagen. He followed Müller's technique, applying the cuff of the apparatus to the arm before the patient went to sleep, and giving him 0·5 gm. of veronal to ensure deep sleep. In this quantity veronal has no effect on the b.p. His findings are confirmatory of Muller's. Indeed, in the case of women, he found exactly the same average systolic b.p., i. e. 88 mm., and while Müller's average for men was 94 mm., Blume's was 95 mm. Among Blume's 20 male patients, there was only 1 whose b.p. departed by more than 5 mm. from the average, being as low as 86 mm. Like Müller, he found that the b.p. during sleep was independent of the b.p. at other times, and, curiously enough, among the 20 women examined, the b.p. during sleep was on the average 1 mm. lower in the subjects of a high waking b.p. than among the women with a comparatively low waking b.p. Blume found that in the case of children the sleeping b.p. is comparatively inconstant. Like Müller, he found that the sleeping b.p. in adults suffering from glomerular nephritis is above normal, whereas it is normal in the subjects of nephroses. C. L.

Morris, N. Anoxaemia and the administration of oxygen. *J. Physiol.*, 1922, **56**, 283.

Mainly animal experiments, with a few observations on cases of pneumonia. Pneumococcal infection does not cause a fall in the total oxygen capacity of the blood. Unilateral pneumothorax, or occlusion of one bronchus produces a fall in the oxygen saturation of the blood, with a small increase in the head of oxygen. Histamine, and induction of asphyxia lead to a decrease in the arterial oxygen saturation, and a fall in the oxygen head. Oxygen administration antecedent to the induction of pneumothorax and continued thereafter prevents any fall in the oxygen saturation of the arterial blood. O. L. V. de W.

Falk, K. G., Noyes, H. M., and **Sugiura, K. Studies on enzyme action. XX. The protease actions of malignant human and rat tumour extracts at different hydrogen-ion concentrations and in the presence of various salts.** *J. Biol. Chem.*, 1922, **53**, 75.

The proteolytic action of extracts of human and rat carcinomas was studied by the Van Slyke amino-nitrogen and the formol methods, in order to see whether there was any special characteristic of the enzymes present. The actions appeared to be tryptic in character having an optimum action at a reaction slightly on the acid side of the reaction of the blood (P_H 7·0). The behaviour to various salts of the proteases from the rat and human sources was similar. R. A. P.

Schmidt, C. L. A., and **Clark, G. W.** **The fate of certain sulphur compounds when fed to the dog.** *J. Biol. Chem.*, 1922, **53**, 193.

Taurine, a constituent of one of the bile acids is excreted in the urine unchanged, and not as taurocarbamic acid. Bile acids when fed are practically not eliminated by the kidney. The fate of other interesting sulphur compounds ingested by the dogs used for experiment is also considered. R. A. P.

Wieland, H., u. **Mayer, R. L.** Der Anteil der Kohlensäure an der Wirkung der Hirnkrampfgifte. [**The part played by carbonic acid in the effect of convulsant poisons.**] *Arch. f. exper. Path. u. Pharmakol.*, 1922, **95**, 5.

Various poisons which have a stimulant action on the respiratory centre, such as camphor, picrotoxin and lobeline, produce in larger doses, when administered to animals, tonic and clonic spasms of the muscles. Now the stimulant action of lobeline on the respiratory centre consists in rendering that centre responsive to tensions of CO_2 to which the centre did not respond before the administration of the poison. The authors regard the convulsant action of these substances as due to the stimulation of a ‘cramp-centre’ in the brain, and they have carried out experiments to determine whether CO_2 plays a part in the action on this centre also. They find, in pigeons, that with moderate doses of picrotoxin, which do not produce convulsions, convulsions can be elicited when an air mixture is breathed containing a percentage of CO_2 above normal. The higher the dose of picrotoxin, the less need be the increase in the percentage of CO_2 above the normal to produce convulsions. They conclude, therefore, that in the action on the cramp-centre, there is the same relation between the poison and the CO_2 in the blood-stream, as in the case of the respiratory centre.

J. H. B.

Cahn, R., u. **Steiner, B.** Über Adrenalin-Resorption und Adrenalin-Wirkung. [**Absorption and action of adrenalin.**] *Jahrb. f. Kinderh.*, 1922, **99**, 44.

In children in whom subcutaneous adrenalin injections produce a rise in the blood-pressure, a rise in the blood-sugar invariably occurs. A marked rise in blood-sugar is also produced in children in whom no rise in the blood-pressure follows the injection. In such children intravenous injection of adrenalin does not produce a pressure rise. Variations in absorption of the adrenalin are not therefore the cause of the variation in the response, as Csépai has suggested from a study of the blood-pressure reaction. Apparently a dissociation of the actions of adrenalin on blood-pressure and blood-sugar exists. O. L. V. de W.

Krontouski, A. A., and **Radzimouska, V. V.** **On the influence of changes of concentration of the $H^{\cdot}$ resp. OH^{1} ions on the life of the tissue-cells of vertebrates.** *J. Physiol.*, 1922, **56**, 275.

The experiments were made on tissue cultures of the rabbit's spleen. Small pieces of spleen were exposed for half an hour to the action of buffered mixtures (lactic acid, acetic acid and borate) of known P_H, and then cultured. The maximum non-lethal concentration of H-ions in lactic mixtures was P_H 4·04, in acetic P_H 5·33. The minimal concentrations of H-ions compatible with life was P_H 10·28. The fibroblasts show the greatest resistance to changes in the reaction. It is clear that such changes in the reaction of the blood as may occur in physiological and pathological conditions cannot kill the spleen cells. O. L. V. de W.

Raiziss, G. W., and Gavron, J. L. A study of the colloidal properties of arsphenamine and allied products. *J. Pharmacol. & Exper. Therap.*, 1922, **20**, 163.

The causes of the 'toxicity' and the reactions following the intravenous injections of arsphenamine are not known. By some it is thought that oxidation takes place with the formation of a so-called arsenoxide, but on the preparation of this compound its toxicity was found not to be so great as anticipated, and Reid Hunt stated that no toxic commercial preparations of arsphenamine have been encountered in which toxicity can be attributed to the presence of the oxide.

The present authors have studied the colloidal properties of salvarsan, and have dialyzed the compound under conditions in which it could not be oxidized. They find that the compound is readily hydrolysed, and on dialysis the chlorine ions had diffused out, and with the sodium salts, sodium passed through the membrane. But with the gold and silver compounds of arsphenamine the metal did not separate from the acid radicle. They believe that it is improbable that the toxicity of these compounds is due to an impurity, but that colloidal investigations may eventually throw light upon the subject.

They maintained solutions of arsphenamine in water in the absence of oxygen for long periods of time. No oxygen was taken up and yet the solutions were markedly changed in toxicity. C. G. L. W.

Schwartze, E. W. The so-called habituation to 'arsenic'. Variation in the toxicity of arsenious oxide. *J. Pharmacol. & Exper. Therap.*, 1922, **20**, 181.

The author has performed a large number of experiments on various classes of animals in an attempt to ascertain the causes of the so-called habituation to 'arsenic'. In the light of the facts presented it is shown that mere consumption of large doses of undissolved arsenious oxide is not proof that habituation exists. But toleration may be due to the relatively low solubility of the compound which is further decreased by the coarse state of sub-division in which it is exhibited.

The writer believes that habituation in higher animals has not been proved, and in the absence of positive proof, and in the face of certain negative results obtained by others, he thinks that the doctrine of habituation to 'arsenic' is open to very serious question. C. G. L. W.

Wolf, C. G. L. The mechanism of the reversal in reaction of a medium which takes place during growth of *B. diphtheriae*. *Biochem. J.*, 1922, **16**, 541.

The reversal of reaction in carbohydrate-free media sown with *B. diphtheriae* is due, in its acid phase, in part to its production of volatile acids. When the media revert to a more alkaline reaction these acids are converted into carbonates. C. G. L. W.

Gibbs, O. S. The oedema of para-phenylenediamine. *J. Pharmacol. & Exper. Therap.*, 1922, **20**, 221.

Para-phenylenediamine is a dye which has been largely used for colouring hair and for dyeing furs, and a number of reports have been furnished of its poisonous qualities.

One of the features of its toxic action is the production of oedema of the head and neck, and also of the tongue, the eyelids and the face. The author has experimented with the toxicity of the dye on cats, and shows that the oedema which has hitherto been observed is the first stage in a general swelling. It is possible that a change in the composition of the blood is responsible for its effect. C. G. L. W.

RADIOLOGY

Radium Therapy.

Werner, R. Die Behandlung von bösartigen Neubildungen mit radio-activen Substanzen. [**Treatment of malignant tumours with radio-active substances.**] *Strahlentherapie*, 1922, **13**, 500–18.

A summary of radium salt technique of malignant conditions, other than gynaecological. Gold or silver tubes of 20–50 mgm. element are used. Superficial applications are arranged in capsule form in concentrations of 10–20 mgm. element per square centimetre; intensification where advisable can be reached by placing tubes behind one another, instead of side by side. Isodoses and skin erythema doses should be calculated for each type and strength of applicator. Distance doses are arranged by interposition of plates of wood, cork, paraffin, &c. Cross-fire, tunneling, and injection techniques are referred to. The biological action of radiation on the different elements of tumours is discussed; in addition to the direct effects—degeneration of the tumour cells and stimulation of the connective tissue—the indirect effects on the vessel-endothelium are important, at first marked dilatation, increased permeability, and surrounding inflammatory and haemorrhagic infiltration being produced, followed by obliteration of the lumen and diminished metabolism in the tissue areas supplied. The centre of the tumour may degenerate, with marked cyst-formation.

With 200 mgm. of radium element one can attain a satisfactory result in a tumour only of middle radiosensitiveness at a depth of 4–5 cm., and by distance applications from 5 cm. With deeper tumours or less sensitiveness only cross-fire can give the result desired. Refractory tumours cannot be well influenced from the surface if they go deeper than 1–2 cm. Combination and alternation of X-ray with radium treatment is often advisable, especially if a case is wholly or in part refractory with one or other agent.

In general the reactions of the skin and other body-tissues to radium applications are as after X-ray treatment, after full doses on skin or mucous membrane 5–6 weeks' interval being necessary.

Tumours in different sites of the body are fully dealt with. Intracranial neoplasms can be treated with 5 cm. distance doses from three or four fields, superficial or intranasal, the former 200–250 mgm. element from 20 sq. cm. area for 24–26 hours each field, the latter 90–100 mgm. element for 8–12 hours (a test exposure being first made as to the mucous membrane sensitiveness). The results with gliomata and gliosarcomata are often excellent, and pressure and other symptoms with carcinoma metastases are often relieved. Pituitary tumours are very favourable, and radium and X-radiation are of equal value here. Retrobulbar gliomata and sarcomata respond well; if distance doses are employed no damage may be anticipated other than perhaps some conjunctivitis or keratitis of slight degree. Prophylactic radiation is too little employed after intracranial and retrobulbar operative measures, in the author's opinion. Superior maxillary lesions are unfavourable for radium treatment if widespread: after operation care must be taken to avoid over-dosage, otherwise osteomyelitis may result, with necrosis of bone. Tonsillar sarcomata and carcinomata of the cheek mucous membrane are treated by cross-fire, in the latter case the sensitiveness is low, but excessive dosage easily leads to necrosis. For tongue and floor of the mouth lesions, cross-fire and combined close and distance doses are advisable. Neck gland tumours frequently react promptly, as anterior and posterior fields can be used: supraclavicular glands, unless markedly prominent, are more difficult to influence well, owing to the restriction to one field.

Oesophageal tumours should all be confirmed pathologically, as they are frequently non-malignant. The technique used is insertion with the oesophagoscope of 30–50 mgm. element for 8–12 hours. Should symptoms of inflammation follow, prompt gastrostomy should be performed. Mammary tumours, from their extent, are usually more suitable for X-ray treatment. Rectal cases should have cross-fire from the sacrum, or in women from the vagina. The reaction is often very marked and colostomy indicated.

Skin epitheliomata, if treated with doses causing marked reactions and crust formation (distance doses being used for deep or extensive lesions), heal in proportions of 80-90 per cent., this being the method of choice, and operation only being carried out in refractory cases. Similar results are found in lip-epitheliomata, the floor of the mouth gland region receiving also full distance doses. J. H. D. W.

Nogier, Th. Radium et radiumthérapie. [**Radium and radium therapy.**] *L'avenir méd.*, 1921, May–October. (*J. de radiol. et d'électrol.*, 1922, **6**, 152.)

Radium is very efficacious in cancer. There are cases of cures which date back more than five years in cases reported inoperable. Surgical statistics in the majority rest on operable cases, therefore favourable, whilst radium therapy statistics rest on desperate cases. When radium is applied to good cases we shall have lasting cures to place beside the best surgical statistics. When the cancer is generalized, neither surgery, radium, nor deep radiotherapy can bring about a cure. One can, however, prolong the life of the patients and relieve them by the use of these methods singly or combined. These methods should be combined, and it is this judicial combination which all the surgeons working on the question of cancer wish for. If radium or X-rays are combined with surgery, the radiations should come first; the inverse method is bad and should be abandoned.

S. E. L.-B.

Schmid, R. Die Strahlentherapie der Myome und der haemorragischen Metropathien seit dem Jahre 1914. [**The radiation treatment of myomata and haemorrhagic metropathies since 1914.**] *Strahlentherapie*, 1922, **13**, 385–430.

This important analysis of radium therapy in benign gynaecological conditions should be consulted by those specially interested, as it gives detailed references to the work of eighteen clinics (indications, technique, and results). Tables are given summarizing the results of radium treatment and X-ray treatment, the latter having been the subject of a previous article. Over 100 references are given to the recent literature. J. H. D. W.

Jacobs, C. Radium considered as the ideal palliative treatment in inoperable cases of uterine cancer and also in cases in which the disease returns after operation. *J. Obst. & Gynaec. Brit. Emp.*, 1922, **29**, 437.

The author points out that the majority who speak of radium in connexion with cancer have the sole idea of a cure in view; he believes that in inoperable cases palliative measures will bring about the same results as palliative surgery, with less risk to the patient. In his paper he does not claim radium as a cure for uterine cancer: the paper deals with cases abandoned as hopeless and post-operative recurrences. In such cases he states that radium can prolong life, arrest pain and discharge, and cause a general improvement in the patients' condition. Six cases are quoted in full in which radium was applied as a palliative; in five of these there was distinct improvement, whilst in the sixth there was no relief.

The effect of radium on the mucous membranes of the uterus and vagina are described and the peculiarities of the scab which forms after treatment. One peculiarity noted is that the leucocytes do not arrive at the area of destruction for some considerable time. The general conclusion is that the principal effect of radium is purely local with no special affinity for the neoplastic cell, a pan-cellular caustic action. The importance of keeping the connective tissue under observation is emphasized and the reasons for so doing explained. The author attributes his success to special care in small technical details. P. L.-B.

Heyman, J. Résultats du traitement des hémorragies climatériques par la radiumthérapie dans la clinique de radium. [**The results of treating climacteric haemorrhage by radium.**] *Acta Radiolog.*, 1922, **1**, 471.

The author states that it is especially in cases of menopausal haemorrhage that radiotherapy has found its place in gynaecology. The question of technique is the one which he considers needs discussing. From 1916–20 57 cases were treated, and of these 52 were examined at a later date. All the 52 cases had severe haemorrhages, treated by other methods without success. He describes what is meant in the paper by favourable results, and his figures in his classification are 92·2 per cent. successes and 7·7 per cent. failures. Referring to the four failures he doubts whether they were due to the method used; one was a haemophiliac, a second received radium treatment after X-rays with favourable results, the third case had an ovarian cyst, and the fourth alone could be classed as a failure, although there was some benefit for a year. Apart from the first three cases mentioned immediately above, treatment was as follows: 1 séance in 41 cases; 2 in 7 cases; and 3 in 1 case.

As regards technique, two methods have been used, (*a*) the intra-uterine application of radium; (*b*) a vaginal application. The method of inserting the tubes is described. Of the 41 cases treated by one séance, 30 were intra-uterine applications and 11 vaginal. The result of both methods is almost the same. Neither method led to complications, but sometimes the malaise after the intra-uterine method was greater than from the vaginal. The results are equally satisfactory, and from the patients' point of view one method has no advantage over the other. Since the distance from the uterine cavity to the ovaries is more constant than that from the vaginal vault to the ovaries the author thinks it more probable that a definite castration dose could be found for the intra-uterine than for the vaginal method.

The number of cases treated are not enough for a comparison between the value of X-rays and radium, but whichever method be used the author believes that a certain and permanent cure can be effected in cases of the type under consideration. P. L.-B.

Radiotherapy

Knox, R. The treatment of gynaecological conditions by X-rays and radium. *Brit. M. J.*, 1922, ii, 678.

At the outset the author states that either X-rays or radium alone, or a combination of the two, may be used in different cases. In general, if the potency of the radiation is the important point, it matters little by which agent it is produced. Since the area treated must receive a certain dose, technique is of great importance, as is also the estimation of the dose, and this needs expert knowledge. The radiation from an X-ray tube or from radium can now be measured very accurately. In deep therapy it is necessary to know what percentage of a beam of rays will reach a certain depth and how much will be absorbed by the tissues; this can be determined by physical means. The third step is to determine what takes place when the radiation reaches the tissues and how it affects the metabolism of the cell. The author thinks that in the future it may be possible to select wave-lengths which will have the maximum effect on a particular type of cell. Reference is made to the fact that different types of cells react differently to irradiation and that Seitz and Wintz introduced their ‘ unit skin dose ’ so as to obtain a uniform method of dosage, from which doses for various conditions have been determined. The author states that too implicit faith should not be placed in the accuracy of the observations as some factors have not been considered.

The technique for treatment of fibromyoma and carcinoma of the uterus has been worked out and is now being generally adopted. X-ray tubes capable of long runs at high voltages are now made and the author thinks that in the future the tendency will be to increase the initial dose and depend more upon it to bring about the desired result. Probably an improvement in the technical use of radium will lead to better results. Radium is most conveniently used for the deep-seated lesions.

Treatment of uterine carcinoma needs expert knowledge, and may need an operation for it to be carried out successfully: the best results are obtained by using both X-rays and radium. The method of irradiating a pelvic growth is described with a small diagram. In order to prevent recurrences the tendency is to increase both the field of irradiation and also the intensity of the radiation: since this has been the case results have improved. A comparison of statistics giving operative and radiation figures is difficult; impartial critics, according to the author, favour operative treatment. Points of comparison between the methods are discussed. The Erlangen method involves great strain on the patient; X-rays are not so successful as surgery in so far as complete removal is concerned. In all suitable cases the author recommends surgery, but he strongly believes in prophylactic X-ray or radium treatment as well. In all inoperable cases it is only a question as to the technique to be used; a combination of the two agents is the best after surgery for all malignant diseases of the pelvic organs; radium is used internally whenever possible and X-rays from without inwards. The radium tubes should be placed within 3 cm. of each other. The lymphatic field must be thoroughly irradiated by X-rays. If. a case is to be operated upon, pre-operative X-ray treatment is not advocated.

The deciding factor as to whether radium or X-rays is to be used is the ease with which it can be applied, since the effect of equal doses of the two agents will be the same. The author believes that gynaecologists will very soon adopt X-ray treatment as a valuable adjunct, and for this reason it is important that they should become familiar with the intricate subject of radiotherapy. Two cases are quoted to show the importance of collaboration with physicians and surgeons, and also of controlling treatment by blood counts at regular intervals.

In conclusion, the author enumerates (1) the contra-indications to treatment by X-rays or radium, (2) the advantages and disadvantages, (3) the dangers.

In the discussion Cecil Rowntree said he had had much better results since he buried radium in the tumour under an anaesthetic, and had not met with any case of vesico-vaginal fistula from the method, but advised ligation of the internal iliac arteries so as to prevent a possible fatal haemorrhage. Prof. Munro Kerr said that X-rays were very valuable in chronic metritis and fibrosis uteri; as regards fibroids, he thought that X-rays might be employed too freely, that hysterectomy was too common, and that myomectomy had not yet attained its proper position. Burrows discussed some less talked of subjects—epithelioma of the vulva, in which he advised operation for all operable cases; menorrhagia in young women, in which he advised curettage first, and, if that failed, exposure to a half-dose system, about 50 mgm. in 24 hours. Farquhar Murray said his experience of radium in carcinoma of the cervix had been most encouraging; he did not favour the X-ray treatment of fibroids. Gamlen said he had always ascertained the exact depth of the growth from the fixed skin areas by inserting an opaque object into the growth and taking stereoscopic radiographs. In reply to a question by Lochrane, Knox said that equally good results could be obtained from radium emanation as from radium; he also agreed that the treatment of leukoplakia of the vulva by radiation was very unsatisfactory.

P. L.-B.

Hertzler, A. E. X-ray and radium in conservative gynaecology. *Am. J. Obst. & Gynec.*, 1922, **4**, 293.

The author thinks that the present trend of the development of the actinic ray therapy should be regarded with consternation. He gives short histories of three cases. In reference to the treatment of myomata by irradiation of the ovaries he says that little mention is made of the suffering of the artificial menopause; he believes that the surgical treatment of myomata is one of the soundest operations in surgery. According to the author, the uterus is the balance wheel of civilization and no method of treatment that leads to a functionless uterus can have a place in modern therapeutics. In all cases the pathology of the tumour should be determined before treatment. The author states that disappearance of the tumour after irradiation is the exception, but some shrinkage occurs in certain cases. As regards the metrorrhagia of adolescence the use of radiation is even less desirable, and sterilization is never warranted as the majority of the cases are due to endocrine disorders. In more than one part of the article the author refers in somewhat scathing terms to the ignorance and incompetence of roentgenologists and radiologists. P. L.-B.

Radiobiology

Hume, Margaret E. The effect of radiation with the mercury-vapour quartz lamp on the growth of rats fed on a diet deficient in vitamin A. *Lancet*, 1922, ii, 1318.

The present experiments were the outcome of work on rickets in infants, conducted in Vienna in conjunction with a number of other workers.

The experiments were devised to ascertain whether any inter-action or mutual substitutability exists between vitamin A and light for the growth of rats, as has been demonstrated to exist between a vitamin factor and light in the case of rickets. If such an inter-action were found to exist the probability of the identity of the antirachitic factor with vitamin A would be heightened. It was also hoped to throw some light on the nature of the inter-action, should it be found to exist.

The mercury-vapour quartz lamp used for the Vienna experiments was of the Hanau pattern; it was always allowed to run for at least five minutes before being used. No estimate was made of its deterioration since purchase, but this was probably great. The lamp used for the Lister Institute experiments was the same as that described by Goldblatt and Soames in the communication which follows. Rats subjected directly to the rays of the lamp were held in the hand, and the head and eyes were shielded either with the hand or with black paper. No untoward symptoms were ever observed, and the dose given was not sufficient to cause a skin reaction. The distance selected was throughout 80 cm. The dose first used was in some cases as much as 20 minutes daily, attained by several steps, but later 10 minutes every second day was used consistently. No attempt was made to ascertain a minimal dose.

The present paper comprises the following experiments:

Group 1. Systematic irradiation of rats fed on a diet deficient in vitamin A; irradiation and deficient diet commencing from the same date. The result of this experiment was that whereas without irradiation growth ceased to be normal after about 7 to 10 days, with irradiation it continued to be normal for from 35 to 50 days. Symptoms of vitamin A deficiency then began to appear and symptoms of xerophthalmia set in earlier than in control animals.

Group 2. Systematic irradiation of rats, long fed on a diet deficient in vitamin A, which had begun to develop eye symptoms. The results appear to show that rats which have been for long (90 days and over) on a diet deficient in vitamin A cannot be recovered, either as regards growth or xerophthalmia, by irradiation with the mercury-vapour quartz lamp.

Group 3. Systematic irradiation of rats which had been, for shorter periods, previously on a diet deficient in vitamin A. Irradiation of rats which had been for shorter periods (17 and 35 days) on a vitamin A deficient diet produced a growth response which appeared to be inversely proportional, in its duration and extent, to the length of the previous period of deficient diet.

The general conclusion drawn is, that there is an inter-action between vitamin A and light for the growth of rats, but that the action of the light is not to produce a photosynthesis of the vitamin. It would appear as if on cessation from normal diet there is a larger or smaller store of vitamin in the rat's body which is for a few days available so that normal growth continues. Very soon, however, it ceases to be thus available; growth almost, but not quite, ceases, and the vitamin store serves the animal for maintenance for a long period of many weeks. At length the store is quite used up, the animal entirely ceases to grow, usually develops severe xerophthalmia, loses weight, and dies. S. R.

Goldblatt, H., and **Soames, K. M. The effect of radiation with the mercury-vapour quartz lamp on the growth of rats fed on a diet deficient in the fat-soluble growth-promoting factor.** *Lancet*, 1922, ii, 1321.

In this paper, it is shown that young rats, if radiated with the mercury-vapour quartz lamp from the time they are put on a diet very deficient in fat-soluble vitamin A grow more rapidly, reach a higher maximum weight, continue to grow for a longer period, and finally, show a general condition better than that of control rats from the same litter receiving the same diet but no radiation. Similar differences between irradiated animals and controls were observed even in the case of a litter of rats brought up by a mother who was fed on the same deficient diet during the latter part of pregnancy and the entire period of lactation.

During the first four or five weeks, despite the deficient diet, the irradiated animals grew at practically the normal rate for rats of that age, but during the next few weeks the rate of growth slowed up definitely, and finally gain in weight ceased altogether. In some of the irradiated animals slight xerophthalmia developed. Rats irradiated when growth has ceased for only a short period, at which time it is conceivable that the entire store of fat-soluble vitamin A is not completely exhausted, resume growth for a short period, then cease gaining weight, and the subsequent history is that of non-irradiated rats on a diet very deficient in vitamin A—viz., decline in weight, and finally death with or without the previous development of xerophthalmia or some intercurrent infection. Some rats whose growth has definitely ceased for two weeks or longer do not resume growth as a result of irradiation, and their subsequent history is unmodified. In some instances decline in weight seems to be accentuated and death hastened by the treatment.

It is apparent from the above findings that radiation with the mercury-vapour quartz lamp cannot act as a substitute for the fat-soluble growth-promoting factor which is a necessary element of the diet. Synthesis of this growth-promoting factor does not occur in rats on a diet deficient in vitamin A as a result of their exposure to radiations from the mercury-vapour lamp. But in some way the above form of light leads to an economy of the action of vitamin A already stored in an animal at the time it is placed on the deficient diet. If the store of vitamin A is not completely exhausted at the time radiations are begun apparently an improvement in appetite and increase of food consumption is generally noted.

The lamp used was a Y 4 pistolette quartz lamp made by the Hewittie Electric Company, using a current of 3·5 amperes and emitting rays whose shortest wave length was 230 mm. The photograph of its spectrum showed particularly dark bands at 258, 312, and 365 mm. This lamp when employed for 15 minutes daily at a distance of 60 cm. was known to prevent the development of rickets in rats receiving a rickets-producing diet.

The above findings agree in most of the essential details with those of the foregoing paper. S. R.

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